Ethical Analysis of Norian XR

(*ENGR 183EW, Summer 2018*) Jonathan Chang

Abstract

Off-label marketing is a crucial regulatory back door in drugs and medical devices due to the FDA's slow approval process. Economic and legal sanctions are insufficient to deter opportunist enterprise. The zeal to tap into new and lucrative markets caused Swiss medical giant Synthes to bypass FDA communication and regulation to enter market research, where experimental devices were tested in production. Even after evidence was obtained proving the dangers of calcium-phosphate based bone-cements in causing blood clots, Synthes executives selectively ignored damaging information with wishful hopes that future successes could justify the product. Patient deaths were not reported to the FDA, or reported in misleading terms that exculpated Synthes. Ethical failures in this company culture of obedience caused at least 5 preventable deaths before the FDA intervened. Stricter economic and legal sanctions, and independent auditing are recommended using deontological and utilitarian analysis.

Contents

1 Acronyms

FDA Food and Drug Administration

CEO chief executive officer

SRS Skeletal Repair System

CRS Craniofacial Repair System

XR (no meaning)

IDE Investigational Device Exemption

VCF vertebral compression fracture

NSAID nonsteroidal anti-inflammatory drug

PMMA poly methyl methacrylate

fMRI functional magnetic resonance imaging

2 Problem Statement

Stringent Food and Drug Administration (FDA) regulations require lengthy clinical trials to prove a significant level of safety before drugs and medical devices are allowed to be tested on human patients. It is therefore common practice to market devices off-label to the health industry, and take the risk of legal penalty as necessary cost of business. Patients are usually notified of participation in experimental drug or device use. However, Synthes had ignored specific warnings from the FDA not to use Norian XR for vertebroplasty, the surgical procedure that treats vertebral compression fracture, obscured or removed required FDA labels, and encouraged surgeons to use Norian illegally, neither notifying them nor the patients of risks involved. This egregious ethical failure led to at least 5 preventable deaths, and the first criminal indictment of executives under the Responsible Corporate Officer Doctrine. While this set legal precedence, sentences were light. Synthes made billions of dollars despite legal sanctions (Kimes, 2012). The corporate structure itself was blameworthy due to the autocratic CEO Hansjorg Wyss and his culture of obediance that made ethical judgments hard – and costly – to exercise. Therefore, prevention requires that Synthes prescribes more open and communicative code of ethics, and also strict FDA legislation to deter future blatant disregard of human life in favor of profits. Ethical analysis demonstrates how Synthes violated moral principles, and how they can be addressed.

3 Background

Swiss surgeons in 1958 founded a research organization to promulgate the then unpopular belief that bones could be treated internally with implants. The products developed were licensed to Swiss manufacturers, branded Synthes. In the 1970s, one founding surgeon struck a deal with Harvard Business School graduate and international businessman Hansjorg Wyss. Wyss soon became CEO of the entire company, which he built into a medical giant with 12,000 employees. In 2011 alone, Synthes generated $4 billion in sales (Kimes, 2012).

In 1999, Wyss found the opportunity to fulfill the original dream in a small company based in Cupertino, CA named Norian. Norian sold FDA-approved calcium-phosphate based bone cement products Norian SRS for the arm, and Norian CRS for the skull. Their novelty lie in that they transform to bone after injection. Synthes bought Norian for $50 million, with intention to use a modified Norian compound for vertebroplasty. FDA representatives said clinical trials were needed to obtain an Investigational Device Exemption (IDE), which would allow Synthes to conduct human tests. A regulatory employee estimated that the process would take 3 years and cost $1 million. Employees interviewed numerous spine surgeons about Norian, and concluded considerable market potential. In zeal, Synthes decided to forgo clinical trial and launch directly into market research. Using a legal loophole for renaming old products, the FDA approved Norian XR, provided that it is also used for the arm or skull. In February, 2000, Synthes pushed strongly for Norian XR to be used in vertebroplasty (Kimes, 2012). **Figure 1** below shows how Norian is to be used. A needle applicator injects bone cement into fractures.

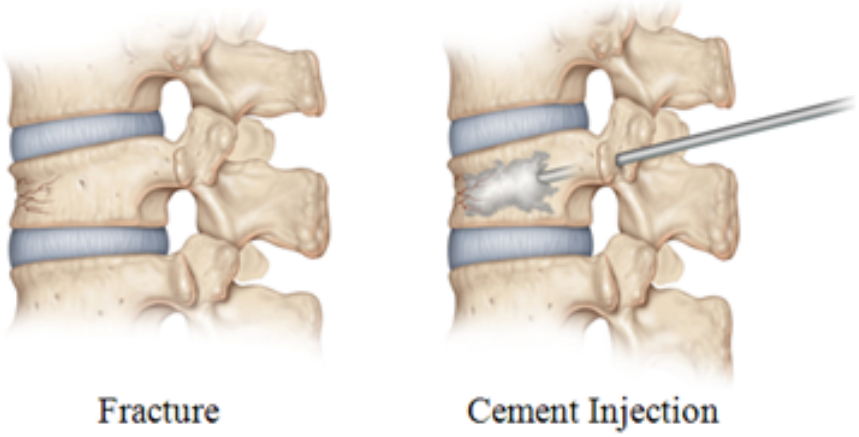

Figure 1: Vertebroplasty (DePuy Synthes Spine, 2018).

Vertebral compression fractures (VCF) are axial load defects prevalent in osteoporotic patients, comprising about half of 1.5 million annual fractures due to bone loss in the U.S. Afflicted patients experience mechanical back pain that worsens when sitting up or standing since the vertebrae supports 80% of body weight. This immobility limits daily task performance for several months. Although the spine naturally heals, it can also be medically managed, avoiding prolonged immobilization, by pain control therapy, using nonsteroidal anti-inflammatory drugs (NSAIDs), opioid narcotics, muscle relaxants, local analgesic patches, or nerve blocks (Wong, 2013). Since the 1990s, patients that do not adhere to conservative treatments are recommended vertebroplasty surgery, usually the injection of poly methyl methacrylate (PMMA) – Plexiglass – bone cement into spinal fractures (Kinkade, 2008). To capitalize on growing popularity of the procedure, doubling from 2001 to 2005 (Gray, 2007), Wyss promoted Norian XR (Kimes, 2012).

The dangers of Norian were well known, both in theory and experiments. Generally accepted theory of blood coagulation states that sudden liberation of nuclease and lipase type protein ferment causes aggregation into fibrin, which is chemically similar to fibrinogen in normal blood. The difference is physical disturbance and liberation of phosphorous and calcium ions (Heard, 1917). More recent studies confirm that polyphosphate enhances blood clots up to 3 times (Smith, 2008), depending on the length of the polymer. Longer molecules ($\geq 500mer$) initiate blood clots, while shorter ones ($\approx 100mer$) accelerate them (Smith, 2010). The presence of polyphosphate and calcium ions actually change fibrin structure, making it more resistant to fibrinolysis, enzymatic clot breakdown (Smith, 2008). Since Norian consists of calcium-phosphate powder (Kimes, 2012), it is, as an external agent, completely free to cause coagulation. Synthes' internal tests, which were subsequently ignored, showed that a pig bled out within 30 seconds of injection due to blood clots, and human blood in test tubes immediately clotted after Norian introduction (Kimes, 2012). Vertebroplasties in general risk leaking bone cement into the spinal canal or blood stream, causing lower body paralysis or fatal blood clots (Wong, 2013); however, doctors found "a relatively small amount of Norian results in the formation of a very large volume of clot" (Kimes, 2012).

The Norian debacle left at least 5 patients dead from routine, optional surgery, caused Norian and parent company Synthes to be fined by Federal prosecution, and the criminal indictment of 4 top executives (Kimes, 2012). The 5 patients were invariably treated for VCF with off-label and unauthorized usage of Norian without being notified of known risks. They are, in chronological order of death, Lois Eskind, Ryoichi Kikuchi, Barbara Marcelino, Reba Golden, and Joan Bryant. Family members of each have filed suits, which have settled or are still in progress (Kimes, 2012).

However, juries have tended to side with the surgeons. Michael Madden, defense lawyer representing Dr. Jens Chapman, who operated on 2 of the patients, and University of Washington, explained that Chapman did not profit from Synthes' enterprise, and has only used Norian in less than 1% of his surgeries (Bellisle, 2016). The jury returned with a 10-2 decision that Golden's death was not due to negligence. Before the decision, Synthes settled for 5% responsibility of $6 million compensation. Separately, for lying to the FDA with intent to defraud, Synthes paid $22.5 million in fines and was forced to sell Norian to Kensey Nash for $22 million. Their total loss was under $1 million. In 2012, Johnson & Johnson acquired Synthes for $21.3 billion, forming DePuy Synthes (Densford, 2016). Since Wyss owned under 50% of the stock, he made about $10 billion, and was legally protected as settlement from the corporate lawsuit. 4 executives Bohner, Higgins, Huggins, and Walsh were sentenced between 5-9 months in prison. They were named in a lawsuit filed by Eva Sloan, Eskind's daughter, who said, "One of the most offensive things was the little piddly sentence they got for this. They could have gone to 7-Eleven and stolen a six-pack of beer and got more time." (Kimes, 2012)

Later studies revealed that despite popularity, vertebroplasties result in no significant baseline or long term differences compared to placebo, if the sham procedure involved local anesthetic and simulated cement injection. A 2016 study, VERTOS IV, found that more than 80% of both vertebroplasty and placebo groups believed that they received actual treatment. Findings replicated an earlier study to suggest that effects in pain and disability management were due to local anesthesia, natural healing, and regression to the mean. However, 12 month post hoc follow up showed vertebroplasties decreased vertical collapse from spine damage (Firanescu, 2018). Similarly, an earlier study showed clinically meaningful pain reduction after procedure, but regressed to no significant difference within 3 months (Kallmes, 2009). Moreover, a long-term follow up of patients of Norian for skull use showed 26% complication rate, mainly infections, with over 80% requiring further surgeries for definitive treatment. The authors suggested correlation between complications and the size of the defects (Gilardino, 2009).

4 Engineering Failure

Human factors may be broken into 4 parties of interest: Hansjorg Wyss, the executives, surgeons, and company employees. Wyss may have been a technology optimist and capital opportunist. The Synthes CEO had come to an understanding from speaking with one of the progenitors be-

fore being offered the position. The original goal of Synthes would have been to treat the spine internally, what Norian XR tried to do (Kimes, 2012). However, a certain callousness and apathy toward human lives must have accompanied the noble goal. After being notified of blood clots, Wyss answered a definitive "no" against clinical trial prospects, and instead suggested a few medical sites to perform 60-80 procedures to help publish results. When Michael Huggins, head of Synthes' North America division, had second thoughts, Wyss reassured him with no room to doubt. When Ken Lambert, medical consultant and orthopedic surgeon who worked with Synthes for decades and was a personal friend of Wyss, expressed the illegality of the strategy, characterizing it as "human experimentation", Wyss discontinued his contract. Yet, when troubles started mounting, he distanced himself from communications, which made him seem less involved (Kimes, 2012).

Synthes executives were loyal and morally passive, too easily swayed by lucrative markets. They initially entered market research after surveying market potential, while ignoring any criticism. It was noted in court records that regulatory employee Michael Sharp was alarmed and sent an email to Tom Higgins, president of Synthes Spine, and Richard Bohner, vice president of operations, when he heard about the plan to promote Norian for VCF. Higgins denied this plan (Kimes, 2012), but soon after marketed Norian to a surgical team led by Dr. Rick Delamarter under UCLA, who performed 2 kyphoplasties on elderly patients. Both their blood pressures dropped, but were kept stable with drugs and survived (Crawley, 2010). No reports to FDA were made. Instead, Higgins organized a focus group to find more interested surgeons, and met University of Washington Drs. Sohail Mirz and Jens Chapman, who suggested animal studies. These studies led to reports of massive blood clots, which were also ignored. Similarly, Lambert's concerns gained little traction. Under executive direction, Synthes tried several times to convince FDA to approve various mixtures of Norian, and ultimately Norian XR. FDA relented, with note that the product should include a warning label against VCF use, or against mixing with barium sulfate, which VCFs require. However, since FDA does not regulate surgeons, these approvals gave Synthes the opportunity to sell Norian to surgeons, then teach them to mix it to perform vertebroplasties. Product manager Josi Hamilton hosted all-expenses-paid golf outings and workshops teaching surgeons how to inject Norian XR in the spine (Kimes, 2012).

Such off-label marketing is illegal, but has long been considered an acceptable cost of business. Since the FDA approval process is too slow, off-label marketing, which short cuts experimental medicine to doctors, is crucial to health care. A 2006 Archives of Internal Medicine study discovered that 20% of examined prescriptions were off-label. Almost all major drug and medical device makers

engage in it, risking billions to settle charges, but the market proves too lucrative. However, patients are usually advised of the risks and grant consent. In order to not run afoul of the FDA, Synthes hid labels and risks from the public. Surgeons usually do not have time to read labels, so Synthes planted a sales representative in every room to monitor the procedures (Kimes, 2012). Mary Crowley, assistant U.S. attorney, argued that "callous disregard of patient safety warrants the highest sentence the law will allow" (Crawley, 2010).

To keep the employees in line, Synthes cultivated a company culture that did not tolerate dissent. Norian product manager Nisra Thongpreda noted that Wyss handpicked young executives from top schools, and cultivated them for loyalty. Wyss was accused of banning employees from using hotel chain Marriott when a worker ignored his request to deliver a banana (Kimes, 2012). This means that employees who asked questions, like Michael Sharp or Ken Lambert, are let go early, leaving behind workers who do as they are told.

In May 11, 2004, FDA investigator Captain Joseph Despins conducted interviews at Synthes. Synthes employees, who had been in panic due to rumors of deaths, still denied everything. Bohner denied knowledge of vertebroplasty test market. Product manager Josi Hamilton disputed off-label marketing. Michael Huggins, head of Synthes' North American division, conveniently forgot all meeting details. Despite so, the particularly diligent Despins filed a 143-page report concluding FDA rule violation, off-label marketing and failure to report deaths to the FDA, and lying to the FDA on numerous accounts (Kimes, 2012). The executives pictured in **Figure 2** below were indicted, along with Tom Higgins, and pleaded guilty.

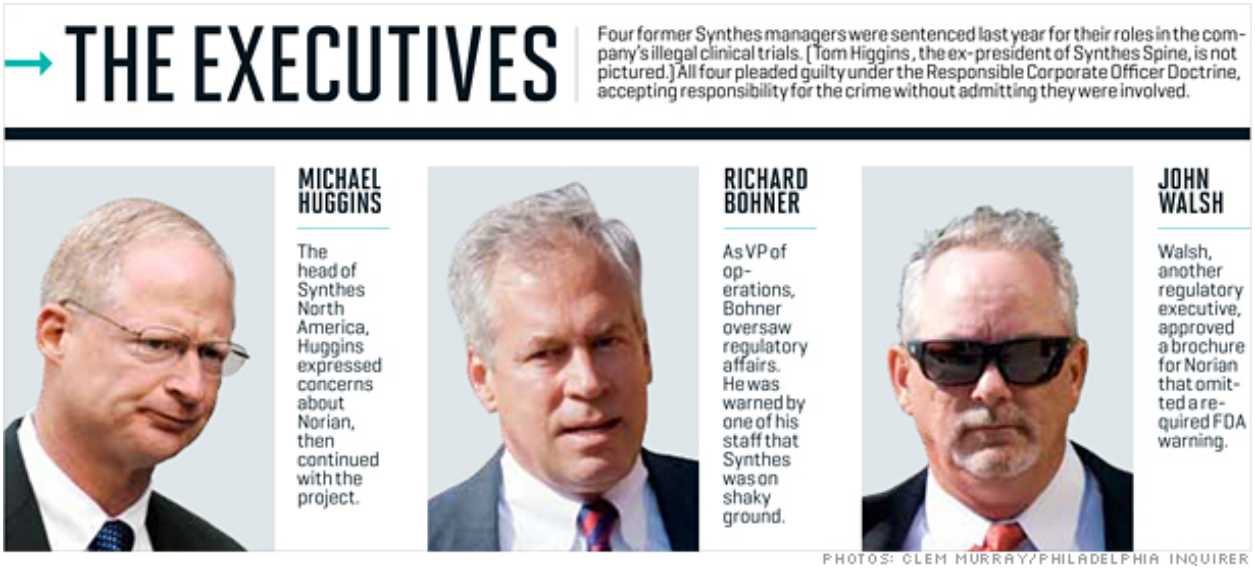

Figure 2: Indicted Synthes executives (Kimes, 2012).

5 Ethical Analysis

Deontology and utilitarianism ethical frameworks are applicable to provide moral references for events, and recommendations for action. The two frameworks are complementary, and should be considered as a balance. Joshua Greene's dual process model, which posits that moral psychology comprises efficient, but inflexible, emotional judgments based on biological factors and inductive experience, and higher-order time-consuming and adaptable rational judgments. This theory was derived from fMRI scans of test subjects contemplating variants of the trolley problem, a hypothetical that asks, essentially, whether it is worth pulling a lever to divert a train and run over one person, or let the train run over 5 without action. Greene noticed that impersonal variants tended to activate the prefrontal cortex, known for deliberative reasoning, while more personal variants (e.g. pushing a fat man to stop the train instead of pulling a lever) tended to activate the amygdala, known for emotive processes. Utilitarianism is more widely justifiable in the former over the latter (Saalfield, 2012). Deontology tends to respect the rights of the minority, which corresponds to not pulling the lever to exculpate the subject from active responsibility of the murder of one, whereas utilitarianism achieves the greatest happiness by saving 5. In Greene's view, deontology and utilitarianism are mutual exclusive processes (Mandal, 2016).

In the medical context, deontology focuses on the patient, while utilitarianism focuses on society (Mandal, 2016). This is none clearer than in the doctor-patient tradition enshrined by the physician's pledge, a modern Hippocratic Oath that serves as a medical industry ethical code. The pledge evokes deontology through 13 rules, detailing the physician's relationship with the patient, including rules such as respecting patient life, autonomy and dignity, well-being, and secrets, regardless of any socio-political factors (Parsa-Parsi, 2017). This can be further demonstrated by a trolley problem variant where the surgeon must decide whether to donate a patient's 5 organs without permission, killing the patient in order to save 5. Deontology notes immediately that this would be unethical prima facie, while depending on the formulation the action may be permissible under utilitarianism under further consideration. Although each framework could be construed in any context, it is by design that deontology protects individuals (e.g. patients) regardless of any societal effect. Unlike utilitarianism, deontology does not account for finite resources, energy, time, and money (Mandal, 2016). Although the theory is debatable, it is widely supported by neurocognitive evidence (Evans, 2013), so it cannot be dismissed off-hand without understanding. The two processes, deontology and utilitarianism, are further analyzed.

Deontology is the study of duty, or obligated actions. These rules are immutable, but may take varying precedence in the event of contradictions. An example of deontology is Kantianism, named after Immanuel Kant. Kant distinguishes moral rules, or categorical imperatives, from hypothetical imperatives. Justifications for action are typically means to some extrinsic end. Suppose a person is hungry, he should then hypothetically eat. In contrast, categorical imperatives are a binding purpose independent of any goal. They have 2 formulations. The universality principle posits that, as actions are independent of the goals of the actor, they must apply to everyone, as universal laws of nature. Therefore, categorical imperatives are maxims that must not contradict when universalized. The reciprocity principle suggests as a maxim that free will should not be denied, since manipulating other people cannot be universalized. Therefore, moral actions must treat others as ends, and not some mean to some other end. From the 2 formulations, it can be derived that since autonomy is desirable, the means by which to exercise autonomy is also desirable. Therefore, knowledge should not be withheld to prevent self-legislation.

Synthes violated each Kantian principle in a number of actions. Executives deliberately withheld information from the FDA and even lied when confronted. It withheld information from surgeons by obscuring pertinent warning labels, and patients by not notifying them that the treatment had not been clinically tested. The maxim that one should lie to the FDA, and obscure safety warnings from surgeons and patients to secure economic and regulatory interests violate the universality principle. In general, to lie and potentially harm others in one's own benefit is self-contradictory as a rule. If the physical harm is universalized, then diminished agency prevents fulfillment of interests. If reputation harm is universalized, in the case of surgeons, then one's diminished reputation might prevent him from being able to influence others, similarly leading to contradiction. By treating others as means to their own interests, Synthes also violated reciprocity. People denied knowledge are unable to fully execute their freedom of will and autonomy. If they had known about the risks, they might have acted differently. Synthes also harmed people who told the truth or did their jobs by terminating employment, and consequently encouraged others to lie or selectively fail in some responsibilities to avoid harm. The maxim of terminating employment when employees make correct ethical choices that jeopardize profits, or in any way coercing against or prevent others from justly performing duties, violates universality. If everyone is prevented from performing duties, then the prevention could not occur. The maxim of using company culture to instill fear and obedience, and stigmatizing whistle blowing, encourages others to violate universality. They are both self-contradictory. These actions also show that Synthes had treated its own employees

as means to ulterior motives, by violating their contracts of employment in good faith. If the employees had known their true work description, they may not have taken the job in the first place. Therefore, Synthes had withheld relevant knowledge and prevented employees from making rational, self-legislative decisions.

Consequentialism is the study of the value of consequences to dictate morality of an action. A well-known formulation is Jeremy Bentham's utilitarianism, whereby each consequence is assigned some utility based on unit amounts of pleasure and pain derived, and the totality of relevant positive and negative consequences are tallied using the hedonistic calculus. Morally right actions have positive utility. Therefore, the utility principle suggests the optimal action leads to the greatest pleasure for the greatest number of people. Utility can be measured by its intensity, duration, certainty, remoteness, and certain other properties. The theory was extended by John Stuart Mill with 2 postulates. The first suggests certain forms of pleasure can be qualitatively more valuable, even if quantitatively less. The second forms the basis of libertarian thought, called the no harm principle, that one should be free to engage in any action if it commits no harm to anyone else. Furthermore, act utilitarianism considers only individual actions, which might be unwieldy, while rule utilitarianism simplifies calculation using moral rules as a kind of expected value for actions.

Ethical failures were also committed from a utilitarian perspective. While numerous decisions could be analyzed, perhaps the most relevant dichotomy is the decision to either bypass clinical trial, lie to the FDA, covertly conducting human experimentation in market research; or, conduct the clinical research and accurately communicate results to the FDA to obtain an IDE, so that market research could be conducted legally. In each event, the stakeholders are Synthes employees, company investors, surgeons and patients, for whom the consequences are relevant. The uncertainty property should be discussed, since even using PMMA cement, there is a small chance of leakage, which causes blood clots. Norian increases this risk, but it still might be small. The lawyer representing Hieu Ball, an involved surgeon, noted that out of 20-30 surgeries he performed using Norian, there was only one death (Kimes, 2012). Using uncertainty, the expected value is 3%-5% of the negative utility of a death. In choosing human experimentation, while harm was not deliberate, the potential of harm was enacted without sufficiently informing the patients; therefore, this can be considered some measure of hostility. The potential for injury, and the almost-certain death when injury occurred, had highly negative utility. The resulting public distrust should also cause negative utility in slight quantity, but spread over a large population. The same qualified hostility can be applied against surgeons, since Synthes was gambling with their reputation and finances,

through potential lawsuits. In most cases, surgeons do not profit from using Norian, although because of this, surgeons have been found innocent in trial. Therefore, the human experimentation is moderately negative to the conscience of a surgeon, or mildly positive to satiate his curiosity. 3%-5% chance of the expense of court trial and insurance costs tilt utility more negative. The negative attention and uncertainty surely had some effect on investors; however, perversely, net profitability skyrocketed nearly every year from 2006-2011, and it was named "HOT STOCKS to WATCH" in 2012 due to the Johnson & Johnson takeover (4-Trader, 2018). It is unclear how much Norian contributed, since the company was successful before Norian. The bone cement business surely contributed to psychological stress of its employees, and at least a couple terminated. A number of executives were named in drawn out court cases that lasted 3 years (Kimes, 2012), with 4 indicted. Aside from legal uses of Norian for arm and skull, which contributed to sales, the attempt to market Norian for VCF caused largely negative or neutral utility for all parties involved. In an optimistic interpretation, if Synthes profitability could be attributed its vertebroplasty activities, there could be some positive offset. However, using Mill's qualitative pleasures, economic benefit of the shareholders must be worth much lower than patients maintaining physical ability, or life. Mill's no harm principle would cement the balance in negative utility between shareholders and patients.

The alternative of achieving a safe product before using it is mildly positive over baseline to patients, since VCFs usually naturally heal over the same time frame as vertebroplasty, as later studies suggested (Firanescu, 2018). Since in the best case, vertebroplasty is optimistically slightly more positive than natural healing, the urgency of Norian cannot be justified from a public safety perspective. A working product is most likely neutral to the general population. To surgeons, it would be largely positive if the trial succeeds in a functional product; however, given knowledge of calcium and phosphate's role in blood coagulation, and the density of blood vessels in the spine, there is large potential for failure. Uncertainty therefore filters positive utility to a moderate quantity. Uncertainty affects shareholders similarly. Since VCF are somewhat common in spine injuries, a successful product would certainly pad stock value. Success may be difficult. If Synthes' other enterprises are successful, it is questionable the effect of Norian on long-term stock outlook. Overall, the potential for failure cancels out the gains of success. Therefore, clinical trials achieve neutral utility for stockholders. The executives, since they avoid prison, benefit in a similar way as stockholders. However, their peace of mind and industry experience without the taint of law secures them mildly positive utility. **Table 1** summarizes the utilities.

Table 1: Utility balance of human experimentation.

	Human experimentation	Clinical trials
Patients	Largely negative	Mildly positive
Surgeons	Moderately negative	Mildly positive
Investors	Mildly Positive	Mildly positive
Executives	Largely negative	Mildly positive

Clearly, the comparison ends favorably for completing proper clinical trials, and obtaining IDE and permission from FDA to conduct market research. There would be either less patient risk, or they would be notified. This would absolve reputation and legal risk from surgeons and executives. Potential effect on stock prices is unknown, although there is a downside and an upside. Overall, Synthes recorded increasing net profitability, which may have been regardless of Norian XR. Analysis has therefore shown that human experimentation would result in moderate to large negative utility, while clinical trials result in mildly positive to neutral utility.

6 Recommendations

The casualties were completely avoidable. To ensure regulatory compliance, Synthes should require independent auditors, instead of internal regulatory employees, to be involved through every stage of communications and management decisions. Since CEO Hansjorg Wyss has a reputation for discouraging dissent and micromanagement, he should step down and let new leadership take company culture to a more open, positive direction that facilitates employee free will toward responsibilities, even if facts emerge contrary to expectations. A degree of unexpectedness is normal, as it implies adherence to reality rather than ideals. Openness and honesty is can be universalized, healthily reciprocated, and encourages autonomous thought and action without necessarily compromising corporate goals. The maxim of complying with regulation through independent audits, free of conflicts of interest, can be universalized without contradiction, since regulations are designed to protect human rights. This resolves the prior maxim of lying to the FDA in perceived self-interest.

Synthes should comply to a code of ethics that places patients first. Although this may limit growth, it ensures long-term sustainability in that the company will usually be considered righteous, becoming a mainstay in the segment it serves. By minimizing harm and injury, and restoring public confidence, it should practically maximize expected utility, at least in a rule utilitarian

sense. Having a code of ethics would also compel employees toward righteous action in order to fulfill their duties. The code of ethics should remind executives to treat patients and surgeons as valuable ends, and other employees to hold the executives accountable by reporting to regulatory auditors as necessary. The maxim to respect others by holding oneself to higher standards can be universalized and reciprocated. Synthes could benefit by broadly applying simple deontological rules to help orient them to a right path.

On the federal level, the FDA must do more to ensure compliance and deter bad behavior. It should enforce not just economic sanctions but legal ones. Blatant disregard of regulation and disrespect to human life should be a felony with sufficient minimum term. Strict, but reasonable, sanctions can be universalized since it encourages proper behavior. The FDA could also apply utilitarianism to this end. The actions are to sanction unethical practices below profitability, or above profitability. The stakeholders are the FDA, the subject company, and the patients. Sanctions below profitability are easy to enforce, so there is positive utility to the FDA. They are not enough to dissuade companies from unethical practices, so in the short term, increased profitability are not offset by legal fines. However, this encourages a culture of bad decisions, and might cause situations like the case of Synthes and Norian XR. The majority of companies may walk a fine line and not commit to any egregious moral blunders, and make it out unscathed. However, disasters may happen. Therefore, it is difficult to commit on whether companies benefit from relaxed legislation. The patients, however, are much suffer much from these offenses, and derive much negative utility. Sanctions above profitability require more diligence from FDA prosecution to press charges. They may greatly jeopardize run-away profits of medical companies, but also save them from grave ethical harm. However, improved public safety is high positive utility. It is notable that strict regulation has potential to save patient lives, whereas FDA risk is political and administrative. Therefore, utility to patients swings much wider. Positive utility of patient safety outweighs negative administrative utility of the FDA and questionable utility to companies. The respective utilities are summarized in **Table 2** below.

Table 2: Utility balance of the strictness of sanctions.

	Sanctions below profitability	Sanctions above profitability
FDA	Mildly positive	Moderately negative
Company	Arguably negative	Arguably positive
Patients	Largely negative	Largely positive

7 Conclusion

The case of Norian XR demonstrates that regulatory realities should be properly addressed, and that proportional care should be invested in products that affect human lives. From both deontological and utilitarian perspectives, it can be shown that moral enterprise has more sustainable profitability in the general case, since imparting positive utility propagates through individuals in society – from patients to shareholders. Promoting open communication with regulatory employees and patients enables the right to autonomous self-jurisdiction. Usually, the interests of one confer the other. Many ethical problems could be solved through responsible cooperation.

In this case, Wyss's propensity towards loyalty and control prevented open communication, cooperation, and autonomy. This, in turn, caused ethical failures that damaged livelihoods and economic profits. Norian XR sets precedent for criminal charges against executives. However, fines were paltry to reasonably deter future opportunists. When the effects of technology become wider and more powerful, ethical responsibility becomes a finer line that must be adhered to. Failures in gene editing might prove far more disastrous consequences. To that end, public and private endeavors must be aligned.

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