

**An Analysis of Ethics in Pharmaceutical Advertising: The Vioxx Case Study**

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Business Ethics – Fall 2012

Final Word Count: 2,798

## Introduction

The role of the pharmaceutical Marketing Manager is a delicate balance of keeping all key stakeholders happy, and maintaining compliance to government rules and regulations, all while increasing the bottom line for the manufacturing company. They use scenario planning as a tool to help make the “right” decisions, but at the end of the day they have the final say in what advertisements go to market and ultimately the safety of the general public. That responsibility requires careful consideration of the forecasted end results and a solid ethical conscious to help guide the final recommendation. The FDA has instilled checks and balances to help keep the pharmaceutical industry honest, but in an effort to not violate freedom of speech, they too have their limitations. With all of these variables in mind, the ethical question at the core of the Vioxx case study is, “Is it morally acceptable to ignore or negotiate findings in FDA warning letters, when doing so can violate an individual’s rights?”

The role of the FDA is to protect the public health by ensuring the safety of foods, drugs, cosmetics, biologics, radiation emitting products, and medical devices. They administer and enforce the Federal Food, Drug, and Cosmetic Act (21 U.S.C. section 301 *et seq.*) which includes broad responsibility from pre-market approval to on-going regulation of marketed products (FDA, 2010). A lot of times the post-marketing regulation is done via randomized reviews (both notified and un-notified) and warning letter notification to the manufacturing company outlining the issues and suggestions to remedy said issues. While the feedback may present itself as a suggestion, the risk of negotiating or non-compliance is significant and can lead to millions of dollars in fines, imprisonment, or even death of a consumer. It is critical that the pharmaceutical manufacturing companies take these letters seriously and react appropriately, keeping in mind their main job to increase revenue for the company, but weighing their

responsibility to the welfare of those who take the drugs and those who are directly (and indirectly) affected by the situation. By not complying with these types of letters, the result can seriously violate the rights of an individual. The Vioxx case study is a great example that showcases the repercussions of not complying with an FDA warning letter.

### **The Vioxx Story**

In May 1999, the FDA approved Vioxx for the treatment of pain and inflammation. Vioxx belongs to a class of agents known as COX-2 inhibitors that work by impeding production of the enzyme cyclooxygenase-2. Vioxx suppresses this enzyme, responsible for producing pain and inflammation, while not inhibiting COX-1, the enzyme involved in the protection of the stomach lining. Inhibition of COX-1 can result in potentially serious consequences, such as stomach ulcers and perforation, which are recognized side effects of other non-steroidal anti-inflammatory drugs (“NSAIDs”) (Green, 2007).

The approval of Merck’s Vioxx led to fierce competition in the analgesic market, going up against Celebrex, an already established COX-2 inhibitor, and many over-the-counter NSAIDs such as Advil and Tylenol, as the best pain solution. In the year 2000, Merck spent \$160.8 million dollars in DTC advertising and simultaneously finished the VIGOR study (Green, 2007). The VIGOR study’s objective was to demonstrate a positive side effect profile, negating the need to carry the gastrointestinal warnings on the drugs label and differentiating itself from the NSAID competition. The VIGOR study was a head-to-head, double-blind, randomized study that showed that Vioxx did indeed have half the GI effects of Naproxen. It also, however, showed that Myocardial Infarction (MI) was five times higher in the Vioxx group than in the Naproxen group. The later finding posed a significant problem for Merck that led to numerous internal discussions around how to proceed based on the findings.

Scientists argued that the higher MI incidence could be explained by Naproxen's cardioprotective effects. This was an even more viable explanation when Merck conducted a second study, where Vioxx was tested against placebo for the treatment of Alzheimer's. This study found zero incidence of MI. On the other hand, there was an established association between Rheumatoid Arthritis and cardiac problems. Ethically, the FDA would not allow a study that tested Vioxx against placebo to evaluate safety since this would put the trial participants at a great risk. On April 25<sup>th</sup> 2000, Merck held a Board meeting to discuss the Vioxx situation and how to handle marketing efforts moving forward (Green, 2007). The outcome of the meeting was that Merck supported their hypothesis that Vioxx did not increase MI, but that the cardioprotective effects of Naproxen caused the increase in MI events. Additionally, Merck received a letter from the FDA in September of 2001 addressing Merck's hypothesis on the MI events and identified that because of the lack of evidence, Vioxx could have potentially caused the MI increase (Green, 2007). Given the data from the VIGOR study, the FDA's documented concerns and knowing the forecasted revenue potential pored with the benefit to Rheumatoid Arthritis patients, what is the morally acceptable marketing response? Should the brand marketing manager ignore the findings and continue to promote the safety of Vioxx, based on a hypothesis? Or should they look for alternative options to help lessen the impact and ensure an ethical solution?

### **Utilitarianism Perspective**

Utilitarianism can be defined as providing the maximum amount of happiness to the population that is affected. It is not majoritarian, because it assesses the weight of the outcomes (DesJardins and McCall, 2005). To view the Vioxx case study in this lens, the argument to keep Vioxx on the market is not only necessary, it's imperative. Patients with RA suffer on a daily

basis and Vioxx provides a superior efficacy profile to help alleviate that pain. Also, these patients tend to have GI side effects, some as serious as ulcers which can require expensive surgical procedures. Economically, these costs compound over time and cause increased insurance costs for the general public. For Merck to do incremental studies and ultimately pull product from the market would not benefit the greater public. In fact, it would cause a detriment.

By keeping Vioxx on the market, the majority of those affected by RA could receive the proper treatment. Merck would continue to see an increase in sales. By withdrawing the drug from the worldwide market immediately, Merck forecasted to take at least a \$2.5 billion blow to revenue (per year), or more than 10% of total expected sales (Appleby and Krantz, 2004). Therefore, to continue to market Vioxx, Merck would grow as a company. Additionally, HCPs could continue to provide a great RA medication with limited GI events, while increasing their own revenues. Economically, this solution would continue to create demand and increase revenues. It would also increase the supply needed, helping the pharmaceutical industry continue to grow. This would be the ideal Utilitarian solution to receipt of an FDA warning letter, providing the maximum amount of happiness to the population affected by the situation.

On the other hand, while MI was only caused in a small percentage of the patients, who are already at a higher risk, the end result can be as serious death. The evidence suggests that the benefit to the majority of those affected is arguably much greater than those who would be at risk for MI. The cost for Merck to do an incremental study to focus on the safety of Vioxx would be very expensive and could cause Merck to pull Vioxx from the market, which would result in a huge hit to their net revenue, and would jeopardize jobs of those who work on the product. Also, the cost to treat an MI patient is significantly higher than the cost to switch therapy or to test in advance for the MI risk.

Alternative options would be to issue a press release that Merck acknowledges the risk to the specific target audience and confirm that they are working with key stakeholders to profile patients in advance of issuing Vioxx therapy, to lessen the risk. Additionally, they could include language in their package insert and fair balance to indicate that Vioxx is contraindicated in high MI risk patients. This would require additional work and education for the sales force to communicate patient profiles with the HCPs and would decrease potential revenue since some patients would no longer be able to use Vioxx. However, it would continue to benefit the majority of those affected in this situation.

From a Utilitarian perspective, Merck should continue to market Vioxx, primarily due to the benefit for people who can receive pain relief from this product with less GI events. This would also keep the Merck Vioxx team employed, and would continue to bring in revenue which would benefit the company, the stockholders and the pharmaceutical industry. There would be some collateral damage to those who have the high MI risk, but in terms of the maximum amount of happiness to those affected by the situation, this would achieve a Utilitarian solution.

### **Individual Rights Perspective**

Every individual has rights and should be treated with dignity and respect. There are different types of rights, such as basic rights (i.e. right the life, speech) and derivative rights (i.e. right to vote or bear arms) (DesJardins and McCall, 2005). The Vioxx case absolutely violated an individual's basic right to life. For those patients who were already at an increased risk of cardiac events, Vioxx increased their chance of presenting with MI and even death. Even though it was a small percentage of patients, it still could cause malice to those people and their families. Economically, the cost to the health system would be lessened by having fewer incidences of MI. The net result of Merck not following the guidance of the FDA warning letter ultimately resulted

in Merck paying 3,468 in death claims to resolve Vioxx suits. A \$4.85 billion settlement fund made payments to the families of 2,878 Vioxx users who died of heart attacks and 590 who died of strokes, according to Lynn Greer of Brown Greer LLP, a law firm in Richmond, Virginia, that analyzed 59,365 claims (Voreacos and Johnson, 2010). Even with the financial compensation, the unnecessary loss of life and the emotional suffering for the survivors could have been avoided if Merck would have acted sooner and complied with the FDA warning letter. The Vioxx team's ignorance to the FDA warning letter violated the 3,468 individual's basic right to life.

Merck recognized that this was a serious problem and they continued to market the product, quelling all safety concerns. They exercised intent to deceive – actually planned to implant a false belief with the HCPs and the patients based on a hypothesis that Vioxx was not responsible for the MI event increase. During the lawsuits, it came to light that Merck drafted dozens of research studies for a best-selling drug, and then lined up prestigious doctors to put their names on the reports before publication (Saul, 2008). Not only does this make the pharmaceutical industry look less valid in the work they produce, but the doctors who agree to put their names on these studies ruined their reputation. Merck argued that these publications actively reflect the respective doctors' opinions but at the end of the day, these doctors have been directly and negatively impacted by supporting Vioxx. The outcome was a deceptive effect, as HCPs continued to prescribe Vioxx for the treatment of RA pain in all patients and the high risk patients continued to present with MI. For the HCPs, the Vioxx team's ignorance to the FDA warning letter also violated their individual rights to effectively practice medicine.

From an individual rights perspective, Merck should have pulled the product from the market to remove the risk to anyone who could potentially be affected by the drug. This would

treat each individual with respect and dignity, showing value for their health and their life. This would however, cause significant impact to Merck and other key stakeholders. The employees who work on the Vioxx account would lose their jobs. Merck's bottom line would suffer greatly which would decrease the company value for stockholders.

Alternatively, Merck's Vioxx marketing team could have invested in scenario planning and forecasting tools to help better address the situation. They could have revised the package insert to call out a subset of patients where Vioxx was contraindicated. Additionally, they could have devoted time and money to helping educate the sales force to work with the HCPs to screen for the MI risk before prescribing Vioxx. This would have shown a level of dignity and respect for the individuals who consume the drug, as well as the HCPs who prescribe it.

### **The Recommendation**

In order to provide a balanced recommendation I reviewed the factual data, the arguments from a Utilitarian and a Rights perspective and also polled a series of people to get a fresh perspective on the case. I used a very small sample size, n of 10, and blinded the product name. A majority of the respondents, 8 of 10, agreed that they would continue to market the product but would have identified ethical alternatives and exercised a number of modifications to ensure the safety and well-being of everyone involved. Not only would this be the morally acceptable response, but it would allow Merck to build a solid reputation in the industry – similar to how Johnson & Johnson handled the Tylenol recall of 1982. What set Tylenol apart from other pharmaceutical recalls? It placed consumers first by recalling 31 million bottles of Tylenol capsules from store shelves and offering replacement product in the safer tablet form free of charge (Rehak, 2002). Johnson & Johnson handled the Tylenol situation from an individual rights perspective. They treated each consumer with dignity and respect.

My recommendation is to continue to market the product, but with a revised package insert to identify this high risk sub segment as a contraindication. Additionally, I would have issued a press release to alert the general public of the situation and to advise that Merck is ethically committed to the safety of all patients. This would not only continue to establish Merck's good reputation but would build trust with the HCPs, patients and stockholders. While it may decrease the revenue in the short term, both the company and the general public would benefit in the long term.

Appropriate patients would be able to continue Vioxx therapy, receiving superior pain relief for their RA with little to no GI side effects. The rights of the high risk patients would not be violated as they would be not appropriate for Vioxx therapy. The Merck Vioxx team would continue to have jobs over the lifetime of the product, and revenue would continue to be made on Vioxx. Merck's company reputation would be valued and the stockholders would be happy. This solution would benefit all key stakeholders and most importantly, it would be a morally acceptable response to receiving an FDA warning letter.

### **Conclusion**

In the Vioxx case study, Merck knowingly and aggressively continued to market the safety of Vioxx even after receiving direction from the FDA that outlined concerns around the product's side effects putting all key stakeholders in jeopardy. The patients who consumed Vioxx were at an increased risk of MI, which can also lead to death, violating a person's basic right to life. As mentioned previously, Vioxx caused 2,878 deaths by heart attack and 590 deaths by stroke, which could have been prevented. The HCPs who prescribed the medication were at an increased risk of losing their license and being sued by those patients who were affected. Those doctors who agreed to put their name on studies they did not conduct ruined their

reputations and were part of the Vioxx trials for years. Finally, the Merck employees and stockholders were at risk of losing their jobs and a major financial impact due to decreased revenue. Merck had to lay off over 5,000 employees, took an annual revenue hit of \$2.5 billion dollars and had a share loss of \$15 per share (Appleby and Krantz, 2004). Other pharmaceutical manufacturing companies should learn from this example, and do what is morally acceptable. They should always err on the side of caution and be slightly conservative, especially when the result can violate an individual's most basic right to life. This would be the morally acceptable response to receiving an FDA warning letter. In the future, the FDA should use this case to help refine their rules, regulations and suggestions to ensure that they too are looking out for the rights of individuals. If there is even the smallest risk of death in post-marketing findings, the FDA should mandate that the company identify the risk and include language in their label and also in the DTC advertising to help eliminate impact to the companies, the doctors and the patients.

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