Ethical Perspective: Ethics in the Pharmaceutical Industry: Vioxx Recall

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The context of this paper examines the industry pressures, that led to the Vioxx Recall in 2004. Current information on the pharmaceutical industry, Federal Legislation and FDA has been updated to provide an ethical perspective comparing the past and present landscape of the industry. During the early 2000's, the pharmaceutical industry is going through difficult times due to the external pressures from society. Some of the factors that have created industry pressures are (1) high cost of pharmaceuticals, (2) medications aren't regulated close enough ensuring they are safe and effective, and (3) consumers lack confidence in pharmaceutical companies, Congress, and governmental agencies. As a result, Congress, pharmaceutical companies, and governmental agencies need to work together as a team to rebuild the confidence of consumers by implementing ethical processes that will drive the pharmaceutical industry in the right direction. By developing, implementing, and evaluation processes to overcome these factors, the pharmaceutical industry can ensure they are doing the right ethical measures to meet the needs of society.

Keywords: ethics, utilitarianism, Kant's Categorical Imperative, FDA, PhRMA, Vioxx, pharmaceutical industry

ETHICAL OVERVIEW OF PHARMACEUTICAL INDUSTRY

Why are ethics in the pharmaceutical industry so important in today's healthcare market? In the past, pharmaceutical companies were once called the "ethical drug companies" and enjoyed the confidence of public support from all members including the physicians who prescribe the medications for patients with the intent to provide benefits (Donlan, 2006). In 2018, based on an analysis of public opinion, pharmaceuticals trust and reputation are eroding. According to recent research, pharmaceutical companies saw a decline of 3.7% from 2017 to 2018. Since the good times, things have changed in regards to the society's scrutiny on the pharmaceutical industry. There is a decline in public's perception of drug companies' authenticity, openness, and transparency because of the changes below (Hu, 2018).

Over the last 20 years, the pharmaceutical industry landscape has changed creating pressure on the pharmaceutical companies. Some off the changes impacting the industry are; (1) an increase in the rising cost to develop and test new drugs has caused companies to create high cost 'blockbuster" drugs with a wider range of treatment options for disease states, (2) social-political pressure has caused a trend towards industry self-regulation resulting in more reliance on corporate compliance policies, (3) aging population has created a challenge on managing healthcare costs for this population within the business environment, (4) increase in high drug costs has caused the greatest criticism within the pharmaceutical industry and, (5) fraudulent scientific research has become a very disturbing trend impacting U.S. Food and Drug Administration (FDA) approval process (Verschoor, 2006).

In 2003, the cost to bring a new "blockbuster" medication to market is greater than $1.2 to $1.3 billion dollars, which has increased significantly since 2001, when the cost was estimated at $800 million dollars (Hileman, 2006). According to Office of the Assistant Secretary for Planning and Evaluation (ASPE), the cost to develop new drugs since 2016 is over $2.5 billion Dollars (2016). Due to these high research and development costs, the pharmaceutical industry is under pressure to be more innovative to market drugs (i.e., orphan drugs) that meet the challenge of rare diseases while being able to manufacture drugs that are affordable to consumers (ASPE, 2016; Donlan, 2006; McKinsey, 2017). Does this mean increase productivity? More funding in R&D? Increase marketing in emerging markets? Since 2004, the pharmaceutical industry is evaluating and developing strategies that provide solutions to develop drugs faster in a more efficient manner to provide consumers lower cost pharmaceuticals (Donlan, 2006 & Kinsley, 2017).

FEDERAL GOVERNMENT AND FDA

Since the 1930's, the pharmaceutical industry has been subjected to increase regulation from the Federal Governments Legislative Congressional branch (Congress and House of Representatives). This pressure has been impacting pharmaceutical companies' business decisions due to the pressure from the public (Carter, 1999; FDA, 2020). As a result of these pressures, Congress believes they have an obligation and duty to represent the public and has an interest to improve the pharmaceutical industry in three areas; (1) reduce pressure from constituents to get drugs for less, (2) address budgetary concerns for constituents utilizing the Federal Medicare and Medicaid programs and, (3) passing laws to promote generics, such as Hatch-Waxman Act of 1984 enabling pharmaceutical companies to submit abbreviated drug applications to the FDA for approval of generic substitutions for brand name drugs. The passing of the Hatch-Waxman has created controversy in the FDA and pharmaceutical companies submitting the generic drug applications. This topic will be further discussed in the paper.

Another agency is the FDA, which is a division within the Federal Government that handles the approval process for pharmaceutical companies resulting in decisions that are a matter of life or death (Congressional Research Service, 2018).

From the years 2000 to 2004, the number of applications submitted to the FDA for approval exceeds the number of staff members available to review the information adequately, resulting in drugs being approved without adequate review. Because of the pressure put on the FDA to review and approve drugs in a timely manner, patents tend to be open for continuous challenge and promising drugs are held up in excessive regulatory review. As a result of the lengthy approval process, it's a trickle-down effect to the pharmaceutical companies to make a profit quickly resulting in potential unethical business decisions (Donlan, 2006).

The pressures put on pharmaceutical companies to develop newer drugs to replace those running off patent to offset the loss of revenue, impacted sales in 2008. Based on annual sales growth over the last 15 years, the percent range between 4 and 7 percent has been consistent. In fact, pharmaceutical companies experienced an all-time low in 2008 sales growth in United States history. According to Intercontinental Marketing Services (IMS) (2007), states "the United States and the five largest European markets, sales growth in 2008 are expected to range from 4 to 5 percent. This marks a historic low for the United States." For 2019 to 2023, annual sales growth is expected to range from 4 to 7 percent in the United States and 3 to 6 percent in the global pharmaceutical market (IQVIA, 2019).

The next section will provide an explanation of ethical theories and how they can be applied towards the pharmaceutical industry will be discussed and utilized throughout the paper to justify both ethical and unethical business decisions. The two ethical theories are Utilitarianism and Kant's Categorical Imperative explain how organizations value those that are near to them and impact how business decisions are made.

ETHICAL THEORIES

First of all, what are ethics? Ethics examines and studies the moral standards of society and individuals to determine whether the established standards are reasonable or unreasonable. Decisions based on the ethical standards start at a young age and develop as we get older. Similar to the influence of society on making moral decisions, these factors impact how we determine the appropriate ethical standards to use in situations or issues that may arise (Velasquez, 2018; Velasquez, 2006).

Secondly, what are business ethics? According to Velasquez (2018), business ethics is "the study of moral standards and how these apply to the social systems and organizations through modern societies produce and distribute goods and services and to the behaviors of the people who work within these organizations." Business ethics applies to organizations, institutions, and behavior. The goal is to achieve two ends: (a) production of the goods (pharmaceuticals) and services (affordable health insurance) that societies want and need, and (b) distribution of the goods and services to the above-mentioned societies (Velasquez, 2018).

How is business ethics applied in the pharmaceutical industry? Business ethics are the result of decisions and actions carried out by individuals within the pharmaceutical industry based on their own established moral standards, norms, and beliefs prior to becoming part of an organization. Because these individuals make up the pharmaceutical corporate structure and governmental agencies, they have their own established moral responsibilities and moral duties. Individual's behavior, choice, and beliefs may be influenced by other employees, corporate policies, corporate norms, and corporate culture, but these corporate artifacts are not responsible for individual actions (Velasquez, 2018).

Utilitarianism

The first of the two ethical theories is the Utilitarian theory. What is Utilitarianism and how is it applied to the pharmaceutical industry? Utilitarian theory bases a decision solely on the outcome (safety of medication) or consequence, by selecting the act (withdraw or recall a medication from market) that provides the greatest social net benefit or the lowest net cost. The net benefit is considered the utility produced by an action. This theory compares cost and benefits and the impact on society. Although, the decision maker may use an act that may not provide the greatest benefit, in the long term the action will provide the greatest social benefit. In the link between individual behavior and ethical decisions, Premeaux explains (2004) that utilitarian decisions are considered unethical when the advantages are at the expense of those affected (i.e., organization, community, people) resulting in undesirable outcomes.

Many organizations, including companies within the pharmaceutical industry utilize a utilitarian cost-benefit analysis when evaluating ethical business decisions (Velasquez, 2018). An example would be the passing of the Hatch-Waxman Act of 1984 by Congress to enable the FDA to accept abbreviated drug applications for generic drug substitutions for brand drugs. Congress believed the decision provided a net benefit to society by saving consumers money on purchasing lower cost medications. Plus, it shortened the process for generic substitutions to be approved through the FDA. Based on this analysis, it was a win-win for pharmaceutical companies developing generic medications (FDA, 2018; Donlan, 2006).

Kant's Categorical Imperative

The second ethical theory is Kant's categorical imperative. What is Kant's Categorical Imperative and how does it apply to the pharmaceutical industry? Kant developed an ethical theory that explains all persons have certain moral rights and duties. Unlike Utilitarian benefits, Kant believes humans possess these rights and duties regardless if the Utilitarian benefits are exercised, such as providing only safe and effective medications to consumers regardless of cost. Kant's theory is based on a moral principle called categorical imperative, which means all persons should be treated equally and treat each other equally. Based on this theory, everyone deserves the right to be treated this way, and everyone has the correlative duty to treat everyone the same way (Velasquez, 2018). In fact, Velasquez (2018) states the categorical imperative and the golden rule have similarities, which is "Do unto others as you would have done unto you."

How does Kant's categorical imperative relate to the pharmaceutical industry? If an individual within a pharmaceutical company chooses a maxim, which is a rule of conduct or principle on which you act in making a decision, such as marketing medication materials based on corporate approved clinical studies (Sage, 2017). Kant's categorical imperative will test whether that maxim is good or bad by asking the question "Is this the same decision everyone else will make?" The next step would determine the relevance, whether this maxim is universal, which means all pharmaceutical companies would perform this action in a similar situation the same way. If so, this means pharmaceutical companies promoting medications solely based on approved clinical information is a good maxim. In today's business environment, pharmaceutical company's maxims would be similar to corporate policies and goals. Unlike employees having the will to make a decision (how to promote a medication), the corporate policies govern the actions of the employees (Altman, 2007).

Based on the two ethical approaches, each theory has its own merits in society and will be applied accordingly to the ethical issues pertaining to the pharmaceutical industry. To better understand how ethics are implemented and utilized within the industry, an overview on the following organizations will be further discussed, including: (1) the Federal Government, (2) pharmaceutical companies, (3) regulatory agencies and, (4) other organizations (PhRMA). The purpose of the next section is to further explain each organization and their impact on society.

ORGANIZATIONAL IMPACT IN THE PHARMACEUTICAL INDUSTRY

Congress

The United States Congress is a legislative part of the United States Federal Government with influential power with pharmaceutical companies, lobbyists, and other governmental agencies. What is Congresses role in our government and impact on the pharmaceutical industry? Key functions of the U.S. Congress are; (1) Congress is the legislative branch given power to write laws pertaining to the pharmaceutical industry, (2) Congress has the authority to tax, impose tariffs, duties, and other measures to collect revenue, (3) Congress also control funds how funds are appropriated and spent in other governmental agencies, such as FDA and United States Patent Office, (4) Congress has power to regulate interstate travel, which covers communication and transportation of people and things across state lines, such as United States Federal Trade Commission and, (5) Congress can exercise supervision over the Executive branch of the government, which is the President and the administration, such as approving laws to benefit the pharmaceutical industry (Congress, 2020).

Congress is a very powerful branch of the federal government having influence over the pharmaceutical companies and other organizations within the pharmaceutical industry. The role of Congress is to work in conjunction with other agencies, such as FDA, the U.S. Patent Office, and Federal Trade Commission (FTC) on creating, modifying, and passing laws to benefit the pharmaceutical industry (Congress, 2020).

Congress passed the Pharmaceutical Drug User Fee Acts (PDUFA) in 1992 due to the pressure from key stakeholders to approve drugs, including pharmaceutical companies, consumers, industry, and the FDA. The PDUFA authorizes the FDA to collect fees (funding) from pharmaceutical companies to review the back log of New Drug Applications (NDA) awaiting approval for the market. The user fees have played a pivotal role in expediting the drug approval process (FDA, 2015). The PDUFA is reauthorized every five years to ensure the FDA and drug sponsors are promoting safe drugs to the marketplace.

The PDUFA includes the following acts passed by congress, including PDUFA I passed in 1992 to provide resources (i.e., hire additional staff to review back-log of NDA) to get lifesaving medications to the market faster, such as AIDS medications. PDUFA II (1997) was modified for additional resources for the FDA drug review process and PDUFA III (2002) revisions focused on improving the review and monitoring of clinical trials (Congress, 2007). PDUFA IV (2007) significantly broadened the agency's drug safety program and facilitated more efficient development of safe and effective new medications for the American public (Congress, 2007) and PDUFA V (2012) passed to provide the necessary resources to maintain an efficient review process for human drug and biologic products that is predictable (FDA, 2016). In 2017, PDUFA VI built on the previous acts to ensure the FDA and drug sponsors are providing safe and

effective medications, included capturing the patients voice in drug development, building a foundation for break through drugs, advancing biomarker therapy, streamline combined product review (biologic and medical device), advancing Model-Informed Drug Development (MIDD) utilizing "real-world" data, and continually hire and retain qualified employees (FDA, 2017).

This PDUFA is an example of how the U.S. Congress and the FDA are working together to ensure things are done in an ethical manner, while continually evaluating, modifying and updating law(s) to accommodate changing times in our society (Yap, 2012).

U.S. Food and Drug Administration

The FDA is another important and influential governmental agency with the authority to make or break a pharmaceutical company's livelihood by approving new drugs, denying potential new drug applications, or recalling an existing drug in the marketplace. The purpose of the FDA and oversight of the pharmaceutical industry is explained in the FDA mission statement (FDA, 2018).

FDA Mission Statement states the FDA protects the public health by assuring the safety and efficacy of human drugs, veterinary drugs, biological products, medical devices, and is responsible for the United States food supply, products that emit radiation, and cosmetics. The mission of the FDA is to regulate the advancement of medicines that are safe, effective, and cost effective for consumers. The FDA helps the public get accurate information that helps improve their health, i.e., science-based television commercials, advertisements, FDA website (FDA, 2018).

In Accordance with the mission statement, the FDA is investing the time and money to make sure they do provide innovated medications to the public that are safe, effective, and improve health. Unfortunately, the credibility of the FDA was questioned in 2004, when the Cox-2 anti-inflammatory drug, Vioxx was recalled. At the time, evidence pointed towards the manufacturer, Merck, for not submitting clinical data from the VIGOR trial that showed an increase in potential cardiovascular events (FDA., 2004). Was this the fault of the FDA for not thoroughly reviewing the clinical data prior to the recall? This created an ethical dilemma with the FDA on how they do business. Based on the FDA's track record since 2000, ten medicines, including Vioxx have been linked to 55,000 deaths according to David Graham, former FDA Research Scientist. In the last 25 years, a total of 16 drugs have been withdrawn, twice as many have "black box" warnings, which alerts physicians and patients about a serve side effect. With so many withdrawals and warnings, one might conclude that the drug approval process is broken in the 100-year-old agency (Herper, 2004; Leaf, 2006). Was the process for drug approval broken or not? According to Leaf (2006), explains the drug approval process is not broken, the FDA's obsession with excessive caution, the delay in drug approval process has impacted the development of life changing medications for diseases, such as multiple sclerosis and Parkinson's, ultimately effecting patients. Also, this obsession for the need of certainty in the drug approval process is killing people by discouraging the pursuit of vaccines for diseases and next generation antibiotics that could save millions of people (Leaf, 2006). Based on the FDA's decision to make changes in the drug approval process to ensure safety is a step in the right direction on making better ethical decisions to protect society, but at what cost is too much safety? If the FDA utilizes the Utilitarian cost-benefit analysis on evaluating these approval process changes, the FDA could find the safety threshold (cost) and the impact on society (benefit). How can the FDA make changes to the drug approval process that are ethically and morally right?

The first step in the process was for Congress and the FDA to review and update the PDUFA provisions, including of the PDUFA IV (20007), PDUFA V (2012), and PDUFA (2017) to ensure additional funds and resources provided to oversee the drug development and review process in an efficient, timely fashion, with predictability. After the Vioxx Recall in 2004, Congress implemented policies that required manufacturers to submit post approval studies, disclose information about ongoing trials and research results, revise product changes in a specific time frame, and high-risk medications may require additional information in the form of a Risk Evaluation and Mitigation Strategy (REMS). These are the necessary steps by the manufacturers and the FDA to ensure safe and effective medications are available for patients. By working together, the FDA and manufacturers can be confident with their ethical decisions of providing additional

funds (cost) to the FDA, which will provide the best possible outcomes for providing society safe and effective medications (benefit) (Wechsler, 2007).

Pharmaceutical Research and Manufacturers of America (PhRMA)

What is PhRMA and how do they impact the pharmaceutical industry? PhRMA was founded in 1958 to represent America's pharmaceutical and biotechnology research companies to help promote public policy dedicated to the discover, modernization, and development of medications to address patient's needs. PhRMA members have invested an estimated $1 Trillion for the discovery and development of new medications and $83 billion for research and development in 2019 (PhRMA, 2020).

PhRMA's mission is focused on winning support in line with public policies that encourage biotechnology and pharmaceutical companies to innovate and develop medications that enhance patients' lives. In order to accomplish PhRMA's mission (2020), by achieving the following: (1) modernizing the drug discovery and development process, (2) promoting value-driven health care, (3) engaging and empowering consumers, and (4) addressing market distortions (PhRMA, 2020).

Similar to the working relationship between the U.S. Congress and the FDA, the pharmaceutical companies and PhRMA are working in conjunction to ensure safe medications are available globally and business decisions are done ethically. After Vioxx recall in 2004, safety has become a focal point in the pharmaceutical industry, which is a high priority shared by the U.S. Congress, FDA, PhRMA, and pharmaceutical companies. As pharmaceutical companies strive to ensure patients receive the safest medications in the U.S., it's also imperative to supply safe medicines to the entire world. In fact, there are over 10,000 medications that are safe and effective available today. As pharmaceutical companies and the FDA play a critical role in monitoring and evaluating the safety of medications, it's imperative to win the American patient's vote of confidence to ensure they are on the right path of re-establishing their favorable reputation (PhRMA, 2020; PhRMA, 2007).

In regards to the scrutiny the public has on the pharmaceutical industry, many have a perception that pharmaceutical companies influence physicians prescribing habits and education based on their relationships. This perception has created a barrage of unwanted publicity for the pharmaceutical industry, which had made pharmaceutical companies less credible creating an unfavorable reputation. What measures need to be implemented to change the public's perceived behavior of the pharmaceutical industry? Prior to the Vioxx recall, PhRMA implemented a code of conduct (ethics) in 2002 that focused on how sales representatives and others marketing pharmaceuticals should interact with health care professionals. Although compliance with the code is voluntary, participation emphasizes that pharmaceutical companies are willing to change business practices that are ethically accepted by the public (Lazarus, 2004).

According to PhRMA (2019), the preamble of the PhRMA code acknowledges that pharmaceutical companies have a concern over the public's perception on how they interact with health care professionals. PhRMA represents pharmaceutical and bio-pharmaceutical companies focused on developing and providing new medicines to patients. The PhRMA code reinforces the interaction between health care professionals and patients to ensure patients benefit and the practice of medicine is enhanced. For example, health care professionals care for patients based on their knowledge and experience with a focus of attending to the patients' medical needs. The PhRMA code is the ethics of care for the pharmaceutical companies to ensure healthcare professionals and patients are provided safe and effective medications while adhering to the highest ethical standards.

To ensure these standards are met, according to the PhRMA code, the following factors addressed are: (1) interacting with health care professionals to share scientific and medical education that supports research to benefit patients, (2) information meetings must be in a venue that's conducive in providing scientific or educational information, (3) informational meetings focus on education and informational exchange and should not provide any entertainment or recreational items, (4) continuing education conference and meetings are independent and cannot be controlled by the pharmaceutical companies in regards to content, faculty, education methods, venue, and materials, (5) Pharmaceutical company support for third-party educational or professional meetings promoting objective scientific and educational activities (6) consultants must serve as a legitimate need for the company and not as reward or compensation for

inducement for prescribing and, (7) Speaker Programs and Speaker Training Meetings educate health care professionals about the benefits, risks and appropriate uses of company medicines. (8) any health care professionals who are members of committees that set formularies or develop clinical practice guidelines need to disclose the relationship with the company to the committee, (9) scholarships and educational funds are allowable, as long as the individuals who will receive the funds is made by the academic or training institution, (10) prohibition of non-educational and practice-related items, i.e., pens, note pads, novelty items with company logo, (11) educational items designed primarily for the education of patients or health care professionals are not of substantial value under $100 per item, (12) Companies that choose to use non-patient identified prescriber data to facilitate communications with health care professionals should use this data responsibly, (13) Independence and Decision Making – no grants, subsidies, scholarships, support, consulting contracts to influence prescribing habits with health care professionals, (14) Training and Conduct of Company Representatives, include applicable laws, regulations and industry codes of practice, and (15) adhere to the PhRMA code (PhRMA, 2019).

Due to the tarnished image of pharmaceutical industry, as these changes are utilized by all pharmaceutical companies, the goal of the improvements is a better image perceived by society on how pharmaceutical companies interact with healthcare professionals.

The FDA also regulates pharmaceutical company sponsored meetings, conferences, and programs. While the FDA, PhRMA, and pharmaceutical companies are all intertwined within the pharmaceutical industry, the FDA has similar ethical guidelines to ensure drug promotions aren't misleading or false. The content of the presentations must provide scientific or educational value, which discusses a fair assessment of the benefits and the risks of the drug. Information must be truthful and only include an FDA indication, which is also known as "on label" (PhRMA, 2019; Lazerus, 2004).

How are pharmaceutical companies adapting to the new PhRMA code of ethics? Most pharmaceutical companies have voluntarily complied with the code in order to change the public's perception on how pharmaceutical companies do business with healthcare professionals. The PhRMA code will bring integrity back in the industry by utilizing scientific clinical information instead of influencing or enticing physicians by free gifts and entertainment. How has the PhRMA code impacted pharmaceutical representative jobs in communicating information to the physicians? Based on a study in 2006, states "an overwhelming 93% of respondents said the guidelines are further limiting access and time with physicians and/or staff and making program recruitment more difficult" (McQuire, 2006). Most pharmaceutical representatives believe the PhRMA code is negatively impacting their job. In the past, pharmaceutical reps would meet with physicians and staff outside the work environment for an opportunity to talk shop without the distractions of the office environment. With implementation of HIPPA guidelines and the PhRMA code, access time with physicians has been greatly reduced. According to McGuire (2006), states 72% of the representatives feel they do not get enough time with physicians, due to the competition with the number of competitor reps.

Based on this survey, what are the positives from the pharmaceutical representative's perspective? Pharmaceutical representatives are becoming more innovative on using scientific clinical data resulting in physicians discussing disease states and patient types more now than in the past. Due to limited access, pharmaceutical representatives believe the Direct to Consumer (DTC) advertising is influencing their jobs, by getting product information in front of consumers, who eventually discuss with physicians (McQuire, 2006).

Implementation of PhRMA code is exactly what the pharmaceutical industry needed to change the public's opinion on how pharmaceutical companies interact with healthcare professionals. As a trade off, the pharmaceutical industry has increased the use of DTC advertising to offset limited access by pharmaceutical representatives. Will DTC advertising impact public opinion? Time will only tell.

Pharmaceutical Companies

Based on the pressures exerted by society in the early 2000's, what was the status in the pharmaceutical industry? Pharmaceutical companies, once profitable and the favorites of investors were experiencing difficult times, including public's concern over the increasing healthcare costs and providing medications that are safe and effective for patients. Today, the same pressures apply to pharmaceutical companies. Over

the last 15 years, pharmaceutical companies have not adhered to the political and public pressures instead of rethinking a number of their strategies, including profits over people (Saltzman, 2019; Verschoor, 2007).

The future has not been very positive for most pharmaceutical companies because of the following reasons, which are; (1) erosion of patent protection has impacted sales growth, such as Pfizer's $13 billion dollar blockbuster Lipitor, (2) increase in copy-cat generic drugs to substitute high cost brand name drugs, (3) industry is finding it difficult to find new blockbusters, with an increase of $186 billion of R&D in 2019 compared $64 billion in R & D in 2006, compared to $27 billion in 1998, resulting in 48 new drugs in 2019, 13 new drugs in 2006, compared to 24 new drugs in 1998 (Jarvis, 2020; Mikulic, 2020) , (4) increased pressure from payers to reduce costs on new and existing drugs and, (5) drugs are being pulled from the market pre and post launch, such as Torcetrapip (cholesterol drug), Vioxx (COX-2 arthritis drug), and Exubra (inhaled diabetes drug) (Bernstein, 2007).

Due to the pressures and reasons stated above, pharmaceutical companies' annual sales growth over the last 15 years has consistently ranged between 4 and 7 percent. In fact, the United States experienced all-time sales growth of 4 to 5 percent in 2008. For 2019 to 2023, the sales growth is expected to be flat with range between 4 to 7 percent compared the global market with 3 to 6 percent annual sales growth (IQVIA, 2019; IMS, 2007).

What are key strategies being implemented by pharmaceutical companies to address these factors? Some of the strategies are; (1) pharmaceutical companies are outsourcing manufacturing operations in India and Asia to reduce overall costs, (2) reduction in work force, (3) mergers and acquisitions, (4) develop R&D innovative strategies to promote newer drugs, discovery, and broader portfolios that cure today's incurable diseases (5) diversify business to hedge risks of prescription business, which includes newer drugs, generics, specialty, consumer health, and orphan drugs, (6) big data on clinical trials to compare one medicine to the competition, i.e., lower health care costs (Linchpin, 2020; Bernstein, 2007).

As a result of the above factors, pharmaceutical companies are taking the public's opinion seriously by improving and implementing strategies to reduce the cost of pharmaceuticals and provide safe medications for all. Based on the ethical theories, pharmaceutical companies, in the past, have operated on a utilitarian approach focusing on profits regardless of benefits to society. Now, pharmaceutical companies are realizing that past decisions have tarnished their reputation and it's imperative to do what's ethically and morally right and win back the public.

VIOXX RECALL CASE STUDY

The final section of this paper will discuss a case study based on Vioxx, manufactured by Merck Pharmaceuticals (Merck). Vioxx Recall case study will provide an overview of the case, actions taken, and the outcome. Based on the information discussed in this case study, a conclusion on whether or not the decision was right or wrong.

Vioxx Recall

Merck has always been a strong leader with many new products developed throughout company history. In the time period 1995-2001, Merck presented 13 major new drugs, including one blockbuster Vioxx, which was approved for marketing in May of 1999. Vioxx is a new type of non-steroidal anti-inflammatory drug (NSAID) called a COX-2 anti-inflammatory pain medication. Due to the competitive nature of this new class of drugs, Merck was competing against Pfizer's blockbuster drugs, Celebrex and Bextra in this billion - dollar market. This class of drugs is thought to be less harmful on the stomach lining compared to the older NSAID medications, while not showing to be any better in relieving pain (Cavusgil, 2007).

In 1999, Merck began the Vioxx Gastrointestinal Outcomes Research (VIGOR) trial to demonstrate whether Vioxx was less damaging on the stomach compared to Naproxen, known to cause adverse events in the gastrointestinal tract. In March 2000, the results of the VIGOR trial showed evidence linking Vioxx to increase in cardiovascular risks. The results showed Vioxx was four times higher than the Naproxen group. At this time, Merck denied these claims and defended Vioxx, stating that no conclusions can be

drawn from the study. However, the FDA felt the results are conclusive and forced Merck to revise the label warning patients of potential cardiovascular risks (Cavusgil, 2007).

What was Merck's decision based on the new data revealed in the VIGOR trial? The executives at Merck decided to stay the course and keep Vioxx in the marketplace. The executive management team considered doing a trial comparing Vioxx to placebo to determine whether Vioxx increased cardiovascular risks. Instead, the executives decided to monitor current clinical trials going on and determine a plan of action after results are available. Merck felt it was unethical to give at risk patients Vioxx or placebo to compare side effects. Of course, was this ethical or not? Based on the VIGOR trial, its apparent Vioxx has a link to cardiovascular risks and would be detrimental to new and existing patients (Cavusgil, 2007).

Did Merck suspect Vioxx posed serious cardiovascular risks? Based on internal company documents, evidence shows that Merck has downplayed Vioxx's alleged risks for years. According to Cavusgil (2007), Merck's former research chief, Edward Scolnick stated to his colleagues in an e-mail that Vioxx's "cardiovascular events are clearly evident (p.454). In fact, upon completion of the VIGOR trial, evidence showed that not only Vioxx, but all COX-2 NSAID inhibitors are at risk for increasing cardiovascular events. To make matters worse, records obtained from the marketing department revealed that sales representatives were instructed to avoid questions from physicians regarding the cardiovascular risks from Vioxx (Cavusgil, 2007).

In 2000, Merck started the APPROVE clinical trial to determine if Vioxx could reduce or prevent or colon polyps. In late 2001, evidence of cardiovascular events appeared early on in the trial, such as heart attacks, strokes, and congestive heart failure (CHF). In the APPROVE trial, Cavusgil (2007) noted the following:

1. In May 2003, clinical data indicated Vioxx patients have a 20% higher chance of cardiovascular risks (heart attack or stroke) compared to patients taking placebos.
2. In November 2003, data indicates the cardiovascular risk increased to a 40% rate.
3. In February 2004, data indicates the cardiovascular risk up to 80%.
4. In September 2004, data indicates the cardiovascular risk has increased to 120% demonstrating the results were statistically significant.

On September 17, 2004, the committee decided to halt the trial. On September 23, 2004, Dr. Kim, Merck's research chief, informed the CEO of Merck, Ray Gilmartin, of the bad news in regards to APPROVE trial results with Vioxx. On September 28, 2004, after evaluating the current status with Vioxx and increased cardiovascular risks, Merck ultimately decided to withdraw Vioxx from the marketplace to ensure patient safety isn't compromised any further (Cavusgil, 2007).

Did Merck make the decision soon enough? According to the FDA (2004), Dr. Lester M. Crawford stated, "Merck did the right thing by promptly reporting these findings to FDA and voluntarily withdrawing the product from the market." Although the FDA thought evidence of cardiovascular risks was very small, the results showed that patients taking Vioxx compared to placebo are at twice the risk of having a heart attack or stroke, the FDA's solution to the problem was to merely monitor all drugs in the COX-2 NSAID class (FDA, 2004).

Based on the FDA and Merck's business decisions for the Vioxx Recall, it's apparent both are to blame for not making the right ethical decision sooner. Merck denied admitting Vioxx caused cardiovascular events because it would reduce sales by billions if the drug was withdrawn. At the same time, the FDA was under scrutiny for not addressing the concern of increased cardiovascular risks in the VIGOR trial in 2000. After four years of continued trials showing Vioxx's increase in cardiovascular risks, the FDA finally issued Public Health Advisory on Vioxx on September 30, 2004, which was two days after Merck voluntarily withdraws Vioxx Cavusgil, 2007).

Based on the 23,000 patients that experienced cardiovascular events (heart attacks and strokes), 13,000 lawsuits have been filed against Merck. Since the Vioxx Recall in 2004, the timeline of significant events on Merck's aftermath:

- In 2005, the first Vioxx case was in a Texas court with a guilty verdict against Merck. Prior to publishing the results of the VIGOR study in NEJM journal, the authors were aware patients were experiencing fatal heart attacks due to Vioxx.

- In 2006, the FDA reviewed external data that demonstrated cardiovascular risks occurred shortly after patients started taking Vioxx.
- According to the data, patients were still experiencing cardiovascular risks after patients stopped taking Vioxx.
- In 2006, the seventh trial begins against Merck in New Jersey. Based out of the six cases, Merck has won 3 and lost 3 cases.
- In 2006, the Lancet journal published research estimating that 38,000 Vioxx patients had heart attacks out of 88,000 patients.
- In 2007, Merck announces a settlement of $4.85 billion to avoid paying the thousands of pending lawsuits, including 47,000 plaintiffs, and about 265 potential class-action cases file. This was one of the largest settlements (Prakash and Valentine, 2007).

In conclusion, the FDA has received an increase in resources for improving the regulatory process of approving medications, reviewing current medications for potential life-threatening adverse events, and ensuring all medications are safe and effective for all patients. For Merck, the outcome wasn't as favorable, due to the millions of lawsuits filed totaling billions of dollars. As Merck's litigation department processes the claims, Merck will think twice about saving a few billion dollars compared to paying billions in restitution for an unethical business decision. If Merck would have treated patients ethically and morally right (Kant's approach), this would have been a favorable outcome. Instead, Merck followed the Utilitarian "Cost-Benefit" approach by putting revenue/profits before patient risks. Because of Merck's ethical decision, has impacted the pharmaceutical industries reputation.

CONCLUSION

In summary, the author's goal of this paper was to provide an overview of the ethics in the pharmaceutical industry. The information included; (a) overview on pharmaceutical industry, (b) social pressure impacting pharmaceutical industry, (c) solution to improve pharmaceutical industry image, (d) explanation of the role of Congress, pharmaceutical companies, and agencies in the pharmaceutical industry, and (e) case study discussing Vioxx Recall.

To gain the public's trust and confidence, the following changes have been implemented over the last 15 years, include; (1) development of RhRMA code of ethics for interacting with healthcare professionals, (1) Congress passing of PDUFA Act for additional funding for the FDA, (3) FDA overall of the regulatory process to ensure safe and effective medications, and (4) passing of the Hatch-Waxman Act to provide generic pharmaceuticals that are affordable to consumers. As time goes on, Congress, pharmaceutical companies, and governmental agencies need to work together in an ethical manner to ensure consumers are provided affordable, effective, and safe medications.

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