DO THE BENEFITS OUTWEIGH THE RISKS? THE LEGAL, BUSINESS, AND ETHICAL RAMIFICATIONS OF PULLING A BLOCKBUSTER DRUG OFF THE MARKET

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I. INTRODUCTION

The pharmaceutical industry has played an important role throughout world history. This industry is responsible for developing, manufacturing, and distributing lifesaving and sustaining medicines. Today, due to medicines developed by the pharmaceutical industry, human beings are living healthier and longer lives. Like most industries, however, the pharmaceutical industry has also been plagued with problems in recent years. Presently, more drugs are being pulled off the market than ever before because of safety concerns. This has been followed by a wave of lawsuits aimed at correcting the error of allowing such drugs on the market in the first place. As a result, the pharmaceutical industry has faced increasing amounts of negative publicity and a lack of confidence from investors and consumers alike.

In the United States, most pharmaceutical companies promote the dual objective of providing health care to the general public while making a profit for their shareholders. This is often a contentious proposition because companies will place a greater priority on achieving the latter rather than the former. Moreover, the irony of this dual objective is that most large pharmaceutical conglomerates, such as Merck, Pfizer, and GlaxoSmithKline, are publicly traded companies.[1] Pharmaceutical companies aim to maximize wealth for their stakeholders (shareholders in the case of a publicly held corporation and owners in the case of a closely held corporation). Therefore, in order to do so,

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[1] *See generally* Yahoo! Finance Home Page, http://finance.yahoo.com (last visited Feb. 15, 2007). Merck, GlaxoSmithKline, and Pfizer stock are traded on the New York Stock Exchange. *Id.*

the objective of every major pharmaceutical company is to produce a blockbuster drug.

Because of the relative importance of producing a blockbuster drug, a withdrawal from the market of this drug can have severe consequences for the respective pharmaceutical company. Subsequently, questions arise as to whether the lure of profit blinded the company into developing a potentially unsafe drug. In answering this question, it is important to examine the legal, business, and ethical ramifications for all parties involved: pharmaceutical companies, federal regulatory agencies, and patients who use the drugs.

This Note will discuss the significant ramifications of withdrawing a blockbuster drug from the market and how such a decision may impact particular persons or entities. Part II will define a blockbuster drug and a subsequent withdrawal from the market. In addition, it will examine the recent growth and role of the pharmaceutical industry in the development of novel blockbuster drugs. Part III will examine the drug approval process in the United States, specifically the steps involved in obtaining Food and Drug Administration ("FDA") approval for a pharmaceutical drug owned by a pharmaceutical company. Part IV will analyze the legal ramifications of withdrawing a drug from the market, discussing recent court decisions involving Baycol and Vioxx. Part V will examine the business effects of such a decision, specifically focusing on how such a decision affects the pharmaceutical industry and the respective pharmaceutical company that is forced to make such a decision. Part VI will examine the ethical considerations that a pharmaceutical company must undertake before making the decision to withdraw a drug from the market. Finally, Part VII and VIII will examine those parties who may be particularly blameworthy in this saga and identify what, if any, potential solutions exist.

II. PHARMACEUTICAL INDUSTRY STATISTICS AND THE BLOCKBUSTER DRUG

The pharmaceutical industry is an ever-growing industry in the U.S. in large part due to the profitability of the blockbuster drug. Because of the synergistic effect that both the pharmaceutical industry and blockbuster drug have on each other, it is important to define a blockbuster drug and its withdrawal from the market. It is equally important to examine the relative importance of the pharmaceutical industry in the United States and its effect on the development and manufacturing of blockbuster drugs.

A. The Blockbuster Drug

For the purposes of this Note, a blockbuster drug is a medicine that generates more than one billion dollars in sales in a year.[2] In 2003, the world phar-

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[2] VISIONGAIN INTELLIGENCE, BLOCKBUSTER DRUGS: A CURRENT ASSESSMENT AND

maceutical market consisted of sixty-seven drugs, which together, generated over $136 billion.[3] Between 2004 and 2009, experts believe that at least twenty-four new blockbuster drugs will emerge, resulting in a total of ninety-three.[4] The current leading blockbuster drug in terms of total sales is Lipitor, which is owned and licensed by Pfizer. For the second quarter of 2006, Lipitor contributed to Pfizer a reported profit of $2.86 billion.[5] In addition, blockbuster drugs are heavily marketed by their respective companies to both patients and health care professionals alike. For instance, as of 2005, Pfizer has spent a total of $16.99 billion on marketing and administration expenses for Lipitor since its inception in the U.S. market.[6] As a result of this heavy marketing, blockbuster drugs such as Lipitor have become well known by the general public. In sum, blockbuster drugs are generally heavily marketed brands that provide patients with the efficacy that cannot usually be provided by generic and arguably less efficacious brands.

B. The Drug Withdrawal

A blockbuster drug withdrawal from the market can be devastating to the respective pharmaceutical company, the patients who use the drug, and the regulatory agencies. A drug withdrawal is either mandated by the FDA (also known as an involuntary withdrawal) or proactively pursued by the drug's pharmaceutical company (also known as a voluntary withdrawal). In the past, there have been instances of both voluntary and involuntary withdrawals. It is important to note, however, that neither a voluntary withdrawal nor a FDA mandated involuntary withdrawal presupposes any innocence or guilt on the part of the pharmaceutical company. Nevertheless, as will be discussed later in this Note[7], a voluntary withdrawal can have much greater consequences in terms of investor relations and public confidence for the respective pharmaceutical company than an involuntary withdrawal.

C. The Pharmaceutical Industry

The pharmaceutical industry's relative importance in the United States is immense. From 2003 to 2004, total sales of prescription drugs increased by

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OUTLOOK FOR CREATING FUTURE BLOCKBUSTERS (2004), http://www.visiongainintelligence.com/reportDetail.aspx?reportId=1088&adSelection=Y&industryIdL1=-1.

[3] *Id.*

[4] *Id.*

[5] Juliann Walsh & Nicole Ostrow, *Pfizer Earns $2.86 Bln on Lipitor Sales; Merck's Profit Slips*, BLOOMBERG.COM, July 21, 2004, http://quote.bloomberg.com/apps/news?pid=10000 103&sid=a1U3vuXKOjwE&refer=us.

[6] *The "Got Cholesterol?" Award: For Overpromoting Expensive Brand-Name Statins*, BITTERPILLAWARDS.ORG, Apr. 26, 2006, http://www.bitterpillawards.org/Crestor-Liptor.php.

[7] *See infra* Part V.

8.3%.[8] Not surprisingly, every year more and more new prescriptions are being written. For instance, the top twenty pharmaceutical corporations and their respective medicines accounted for approximately $2.5 billion dispensed prescriptions.[9] In addition, the pharmaceutical industry netted a total of $235 billion in industry sales in 2004, which was nearly nineteen billion dollars more than the previous year.[10] The desire to obtain a "piece of this pie" is motivating pharmaceutical companies to spend more in research and development than ever before.[11] In correlation with an increase in research and development expenditures by pharmaceutical companies, retail spending on prescription drugs has increased significantly. As a result, "pharmaceuticals accounted for nearly one in every ten dollars spent on health care," a number that is projected to rise to nearly fourteen percent of all health care costs by 2010.[12]

1. Ongoing Debate Between Pharmaceutical Industry Proponents and Its Critics

Proponents of the pharmaceutical industry claim that the industry is simply supplying the market demand for its goods. Critics, however, point to the fact that there are several competing drugs in each category and question why the industry produces so many duplicates, rather than focusing on the development of novel medicines.[13] Critics, including many consumer advocacy and watchdog groups, point to classes of drugs such as statins, as the problem.[14]

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[8] *2004 Year-End U.S. Prescription and Sales Information and Commentary*, IMSHEALTH.COM, Feb. 22, 2006, http://www.imshealth.com/ims/portal/front/articleC/0,2777,6599_3665_69890098,00.html [hereinafter *2004 Year-End*].

[9] IMSHealth.com, Leading 20 Corporations by Total U.S. Dispensed Prescriptions, 2005, http://www.imshealth.com/ims/portal/front/articleC/0,2777,6599_73914140_77266121,00.html.

[10] *2004 Year-End, supra* note 8. The net total of $235 billion was calculated by adding the following: chain stores, mail services, independent non-federal facilities, clinics, food stores, long-term care, federal facilities, home health, HMO, and other categories. *Id.*

[11] *Id.* In 2005, the biopharmaceutical industry spent a total of $51.3 billion in research and development. PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA, PHARMACEUTICAL INDUSTRY PROFILE 2006 10 (2006) [hereinafter PHARMACEUTICAL INDUSTRY PROFILE 2006].

[12] MERRILL GOOZNER, THE $800 MILLION PILL: THE TRUTH BEHIND THE COST OF NEW DRUGS 232 (2004).

[13] Drugs are often categorized by the disease-state that they attempt to treat.

[14] Omudhome Ogbru, Statins, http://www.medicinenet.com/statins/article.htm (last visited Feb. 15, 2007). "'Statins' are a class of drugs that lowers the level of cholesterol in the blood by reducing the production of cholesterol by the liver. Statins block the enzyme in the liver that is responsible for making cholesterol. . . .Statins are used for preventing and treating atherosclerosis that causes chest pain, heart attacks, strokes, and intermittent claudication in individuals who have or are at risk for atherosclerosis." *Id.* The most popular statins include Lipitor, Zocor and Pravachol, which are also three of the highest selling drugs within the pharmaceutical industry. *2004 Year-End, supra* note 8. The statin class of drugs currently accounts

Industry critics believe that the lure of profits and the subsequent investor perception has led companies to produce drugs that increase revenues rather than those that benefit the general public by treating an incurable or untreatable disease.[15] Why else would there be a number of drugs in the same class that perform virtually the same function?[16]

In response, many proponents of the pharmaceutical industry rebut such a argument by claiming that each drug in a category, although created to treat the same disease-state, often has a different mechanism of action and as a result is in fact a novel drug.[17] The practical answer, however, is that each drug makes a lot of money.[18] As blockbuster drugs, these drugs can single-handedly reverse the fortunes of any dwindling pharmaceutical company. In other cases they may further enhance the profitability at a successful pharmaceutical conglomerate, certainly increasing its worth on Wall Street.

2. *The Pharmaceutical Industry's Reliance on the Blockbuster Drug*

Blockbuster drugs account for a large percentage of the total net sales produced by the pharmaceutical industry. These drugs dominate the market because of their relative popularity and overall efficacy and safety.[19] In 2004, the top ten blockbuster drugs accounted for nearly thirty-eight billion dollars of total sales.[20] In 2004, for example, the top ten selling drugs in the United States made more than two billion dollars in sales each for their respective companies with the leader being Pfizer's statin, Lipitor, which accounted for $7.7 billion in sales.[21] These extraordinarily high returns indicate that the pharmaceutical companies clearly have a vested interest in ensuring that their blockbuster drugs remain on the market.[22]

There is a downside to keeping a problematic blockbuster drug on the market. Keeping such a drug on the market may cost the pharmaceutical company millions, even billions, of dollars in lawsuits, negative public perception,

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for the largest sales volumes in the industry. *Id.*

[15] *See* Merrill Matthews, Jr., *Drug Company Profits Aren't a Problem—They're the Solution*, HEALTH CARE NEWS, July 1, 2001, http://www.heartland.org/Article.cfm?artId=640.

[16] GOOZNER, *supra* note 12, at 229.

[17] Ogbru, *supra* note 14. For example, "[s]tatins differ in several ways. The most obvious difference is in their ability to reduce cholesterol." *Id.* They also differ in terms of their mechanism of action and chemical structure. *Id.* A few of the statins "are completely synthetic and have chemical structures that differ greatly from the natural statins." *Id.*

[18] Walsh & Ostrow, *supra* note 5.

[19] Catherine Arnst et al., *The Waning of the Blockbuster Drug*, BUS.WK. ONLINE, Oct. 18, 2004, http://www.businessweek.com/magazine/content/04_42/b3904034_mz011.htm.

[20] *2004 Year-End*, *supra* note 8.

[21] *Id.*

[22] It should be noted that although a blockbuster drug accounts for sales in excess of one billion dollars, it is difficult to compare a blockbuster drug to a non-blockbuster drug because the latter's sales can vary due to a number of factors, such as with respect to its relative popularity and associated disease-state.

and decreased investor confidence. More importantly, the pharmaceutical company's inaction may have a negative impact on the health of patients who use and rely on the drug in the first place.

The cost of a failed blockbuster drug can be especially devastating for pharmaceutical companies that require successful blockbuster drugs in order to recoup the high cost of developing and manufacturing these drugs. In addition, although the pharmaceutical industry enjoyed a 5.4% increase in sales in 2005,[23] this number is significantly lower than the 8.3% increase the industry enjoyed in 2004.[24] Although the current growth rate is still a strong number, the withdrawal of blockbuster drugs Vioxx and Bextra contributed to the declining growth from previous years.[25] Therefore, both the pharmaceutical industry and its companies require a blockbuster drug to succeed commercially, specifically before the company loses its right to exclusive marketing of the drug[26] or the drug's patent expiration[27], in order for the pharmaceutical industry to enjoy a strong growth rate and for its companies to recoup their investment in development and manufacturing of these drugs.

3. *The Evolving and Future Role of the Pharmaceutical Industry*

Furthermore, prescription drugs have played an increasingly important role over the years, especially as the United States' population ages.[28] According to the Administration on Aging, the older-aged segment of the United States' population is growing substantially.[29] In addition, many of those reaching the age of retirement will live 18.2 years longer than their predecessors.[30] According to these statistics, medications produced by the pharmaceutical industry have helped to sustain the lives of the octogenarian demographic. Therefore, as a significant portion of the population grows older, the pharmaceutical industry will be placed under greater scrutiny to ensure that the drugs that are

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[23] *IMS Health Reports 5.4 Percent Dollar Growth in 2005 U.S. Prescription Sales,* IMSHEALTH.COM, Feb. 22, 2006, http://www.imshealth.com/ims/portal/front/articleC/0,2777,6599_3665_77180090,00.html [hereinafter *Percent Dollar Growth*].

[24] *2004 Year-End, supra* note 8.

[25] *Percent Dollar Growth, supra* note 23.

[26] *See* 21 C.F.R. § 314.108 (2006).

[27] Generally, a drug's patent expires after twenty years, although this number can vary due to a host of other factors. *See* FDA.gov, Frequently Asked Questions on Patents and Exclusivity, http://www.fda.gov/cder/ob/faqs.htm#How%20many%20years%20is%20a%20patent%20granted%20for? (last visited Feb. 15, 2007).

[28] *See generally* ADMIN. ON AGING, U.S. DEP'T OF HEALTH & HUMAN SERVS., A PROFILE OF OLDER AMERICANS: 2004 *passim* (2004), *available at* http://www.aoa.gov/prof/Statistics/profile/2004/2004profile.pdf.

[29] *Id.* In 2003, over two million persons reached age sixty-five. *Id.* That same year, 1.8 million persons of age sixty-five or older died, which resulted in an annual net increase in the senior population of over 317,000. *Id.*

[30] *Id.*

being produced are safe, as well as efficacious. Thus, as the number of drug withdrawals increases, this demographic is affected more than any other.

III. FDA DRUG APPROVAL PROCESS

Presently, there is mounting internal and external pressure placed on pharmaceutical companies to produce blockbuster drugs. Internally, management understands that profitable drugs are needed in order to finance other operations, as is the case in many businesses. On the other hand, externally, shareholders want novel blockbuster drugs because that often corresponds to increased profitability and as a result a simultaneous increase in dividend payments. Because the average blockbuster drug's return on investment is only five percent, the large pharmaceutical conglomerates would need to produce two or three blockbuster drugs per year in order to grow sales by ten percent.[31] Although such a number may seem absurd, especially considering that it costs hundreds of millions of dollars to produce a blockbuster drug, the pharmaceutical industry has in fact sustained such a pace. The number of blockbuster drugs on the market has increased from seventeen in 1995 to sixty-seven in 2003.[32] Just as the number of blockbuster drug brands have increased, so too has the number of blockbuster drug withdrawals. As a result, the FDA's drug approval process has come under scrutiny by many experts.[33] Even the agency that dictates whether a drug is fit for introduction into the open market is not immune from criticism, especially when its self-acclaimed stringent drug approval process fails to uncover the drug's safety problems.

The drug approval process within the FDA is still a rigorous process that consists of several phases of testing. [34] Regulation of a new drug is performed by the Center for Drug Evaluation and Research, a branch of the FDA.[35] The process for approval begins by requiring the pharmaceutical company to take steps to perform pre-clinical screening of the drug in order to prove through their subsequent submission of data to the FDA that the drug is reasonably safe.[36] In order to ensure that the drug is safe, during preclinical drug develop-

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[31] Beyond the Blockbuster Drug: Strategies for Nichebuster Drugs, Targeted Therapies and Personalized Medicine, BUS. INSIGHTS, Feb. 2005, *available at* http://www.researchandmarkets.com/reports/295612.

[32] Visiongain, *Blockbuster Drugs Expected to Rise by 93% to $262 Billion by 2009 Predicts Visiongain*, PR9.NET, Nov. 15, 2004, http://www.pr9.net/health/medicine/1322 november.html.

[33] Christopher Placitella & Justin Klein, *The Civil Justice System Bridges the Great Divide in Consumer Protection*, 43 DUQ. L. REV. 219, 220 (2005).

[34] FOOD & DRUG ADMIN., U.S. DEP'T. OF HEALTH & HUMAN SERVS., CENTER FOR DRUG EVALUATION AND RESEARCH HANDBOOK *passim* (1998), *available at* http://www.fda.gov/cder/handbook/.

[35] *Id.*

[36] *Id.* Before the FDA allows the pharmaceutical company to use a drug or compound, in further initial, small scale pre-clinical studies, the pharmaceutical company must put forth

ment, the pharmaceutical company must evaluate the drug's toxic and pharmacologic effects by conducting short- and long- term testing on animals. Only if the drug passes the requirements of pre-clinical screening, will it undergo a series of additional screening phases.[37]

During the next three phases, the drug is tested vigorously in order to ensure its efficacy and safety. For instance, during the first phase, the drug is introduced and administered to humans.[38] These studies are closely monitored and are usually conducted with healthy volunteer subjects.[39] The object of these studies is to determine the metabolic and pharmacologic action of the drug in humans, including any potential side effects associated with increasing doses (if available).[40] During the second phase, early controlled clinical studies help determine the common side effects and risks associated with the drug.[41] Finally, during the third phase, the effectiveness of the drug and the overall benefit-risk relationship of the drug are evaluated.[42]

Although the FDA's drug approval process is stringent, the pressure to produce more blockbuster drugs has caused pharmaceutical companies to submit an increasing number of applications for new drug approval to the FDA.[43] Requiring a thorough evaluation of each drug has put a considerable strain on the FDA due to its lack of resources and manpower.[44] Moreover, lobbying efforts by the pharmaceutical industry have since convinced Congress to amend earlier statutes that previously required nearly fifteen years of FDA testing for approval of a new drug.[45] For example, in response to serious epidemics such as AIDS, the FDA reduced the amount of time for reviewing a new drug to between six and twelve months.[46] Congress officially reduced the review time in 1992, when the Prescription Drug User Fee Act was passed in order to expedite

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data that the drug-compound is reasonably safe.

[37] *Id.* During these phases, the new drug is screened for efficacy and safety through a series of clinically monitored trials. *Id.* "A clinical trial is a research study designed to answer specific questions about vaccines or new therapies or new ways of using known treatments." The Open Door Clinic, Definitions of HIV Glossary, www.opendoorclinic.org/hivglossary.htm (last visited Feb. 16, 2007). In essence, "[c]linical trials (also called medical research and research studies) are used to determine whether new drugs or treatments are both safe and effective. Carefully conducted clinical trials are the fastest and safest way to find treatments that work in people." *Id.*

[38] RICK NG, DRUGS: FROM DISCOVERY TO APPROVAL 144 (2004); *see also* FOOD & DRUG ADMIN., *supra* note 34.

[39] FOOD & DRUG ADMIN., *supra* note 34.

[40] *Id.*

[41] NG, *supra* note 38, at 145-46; *see also* FOOD & DRUG ADMIN., *supra* note 34.

[42] NG, *supra* note 38, at 146; *see also* FOOD & DRUG ADMIN., *supra* note 34.

[43] *See* Deborah G. Parver, Note & Comment, *Expediting the Drug Approval Process: An Analysis of the FDA Modernization Act of 1997*, 51 ADMIN. L. REV. 1249, 1249-53 (1999).

[44] *See id.* at 1255.

[45] *See id.* at 1253, 1255.

[46] NG, *supra* note 38, at 164 (stating that Merck's AIDS drug, Crixivan, was approved in just forty-two days).

the drug approval process.[47] Curiously, although the amount of time required to review a drug has decreased, the number of drug withdrawals has continued to rise. The remaining question is whether there is a direct correlation between the reduced amount of review time and the increased number of drug withdrawals in recent years.

According to the Pharmaceutical Research and Manufacturers Association ("PhRMA"), an organization comprised of representatives from a number of pharmaceutical companies, there are significant costs associated with producing a blockbuster drug and bringing it to market.[48] Generally, the industry responds to claims that the drug approval process is not stringent enough by pointing to the substantial amount of resources invested in producing a blockbuster drug.[49] The industry claims that pharmaceutical companies have a considerable stake in producing a drug that is both safe and efficacious. For instance, a blockbuster drug costs a pharmaceutical company an average of over $800 million dollars to develop from its infancy as a molecule.[50] In addition, of the five to ten thousand chemically synthesized molecules examined by the FDA, only one ever becomes an approved drug.[51] Therefore, it could be argued that the pharmaceutical industry is more than committed to producing safe drugs, which can be directly attributed to the great number of drugs that are discarded due to problems in the earlier stages of development.

Regardless of these statistics, however, the alarming rise in the number of blockbuster drug withdrawals has caused many critics to "point the finger" at the FDA's reduced review time. During the 2004 Senate Finance Committee Hearings concerning the drug Vioxx, Doctor David Graham, the Associate Director for Science and Medicine in the FDA's Office of Drug Safety, called the FDA incapable of protecting the American public from another blockbuster withdrawal such as Vioxx.[52] He claimed that FDA officials pandered to the

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[47] *Id.*; *see also* CTR. FOR DRUG EVALUATION & RESEARCH, U.S. FOOD & DRUG ADMIN., PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES (2005), *available at* http://www.fda.gov/cder/news/pdufagoals.htm. The Prescription Drug Fee Act required pharmaceutical companies to pay a fee to the FDA before commencement of a review of the respective company's new drug application. This fee was used to hire more reviewers and scientists in an effort to streamline the process and resulted in a new timeline for review consisting of only seven years. *Id.*

[48] PHARMACEUTICAL INDUSTRY PROFILE 2006, *supra* note 11.

[49] *Id.*; *but cf.* Marcia Angell, *The Truth about the Drug Companies*, THE N.Y. REV. OF BKS., July 15, 2004, *available at* http://www.nybooks.com/articles/17244 (claiming the cost to develop a blockbuster drug is not as great as is claimed by the pharmaceutical industry).

[50] PHARMACEUTICAL INDUSTRY PROFILE 2006, *supra* note 11; *contra* Angell, *supra* note 49.

[51] J. Michael Hayes, The United States Drug Approval Process, at 3, http://www.continuingeducation.com/pharmtech/drapproval/drapproval.pdf?x=1141768340&t= (last visited Feb. 16, 2007). All drugs are created from chemically synthesized molecules. *Id.* The mechanism of action of a molecule differs from one drug to another, even if they are from the same class of drugs. *See id.*

[52] Placitella & Klein, *supra* note 33.

wishes of big pharmaceutical companies, even so far as allegedly attempting to pressure him into changing his scientific conclusions and recommendations regarding certain drugs.[53] The Journal of the American Medical Association ("JAMA") agreed with Doctor Graham and claimed that the FDA's post-market-approval-surveillance system was underfunded and understaffed. This shortage of adequate finances and manpower has led to thousands of deaths each year by drugs that should have been withdrawn in the first place.[54]

Further proof can be found by examining the FDA drug approval process, which would reveal that although the process is stringent, in the past it has failed to weed out those drugs that were unsafe to place on the market. In addition, the heavy price tag placed on the development of each molecule increases the incentive for the pharmaceutical company to push the drug to market, especially if the drug is in the third phase of testing. Often times in the third phase, the drug is viewed as an eventual release to the market and is often portrayed as such by the company. In doing so, the company's stock price increases as the company is viewed as having a strong pipeline that may lead to a more financially prosperous future.

Conversely, loss of such a drug during the third phase can be devastating financially and publicly for the company and its shareholders. In recent years, several high profile drugs have been pulled off the market due to safety concerns. A withdrawal of a blockbuster drug may not only affect the company financially and legally, but can also affect its public image.

Therefore, the withdrawal of a blockbuster drug from the market can have a direct effect on not only the respective pharmaceutical company and its consumers, but also the FDA and other agencies that failed to prevent the drug from being introduced on the open market. It seems apparent from recent drug withdrawals that as the number of blockbuster drugs pulled off the market increases, the FDA's drug approval process will come under continued scrutiny. This may ultimately lead to significant changes in the way the FDA handles new drug applications.

IV. LEGAL RAMIFICATIONS OF PULLING A DRUG OFF THE MARKET

When a pharmaceutical company pulls a drug off the market as a result of an FDA mandate, it is in many cases conceding that the drug was somehow flawed. Usually the flaw or flaws in a prescription drug pulled off the market can be attributed to safety concerns. In recent years, several high profile blockbuster drugs, such as Rezulin and Baycol, have been pulled off the market for just this reason.[55] Many of these recently withdrawn drugs were used to treat a

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[53] *Id.* at 220-21.

[54] *Id.* at 221.

[55] Parke-Davis/Warner-Lambert Inc. (currently owned by Pfizer) voluntarily withdrew Rezulin from the U.S. market in 2000. Jim Morris, *Diabetes Drug Rezulin Taken off Market:*

wide variety of disease-states.[56] In such cases, patients and health care professionals had to find alternatives to treat these life altering diseases. Conversely, the pharmaceutical companies that manufactured drugs, such as Rezulin and Baycol,[57] were inundated by a number of lawsuits. Both companies are currently fighting the majority of these lawsuits domestically and globally.

The legal ramifications of pulling a blockbuster drug off the market may be significant for both the plaintiff and the defendant-pharmaceutical company. First, a verdict against a pharmaceutical company can lead to large jury awards, specifically punitive damages. A pattern of such losses and large awards can lead to more lawsuits, including class action lawsuits, which may financially burden the company for a long time. It may also lead to a global settlement in order to prevent the company from going bankrupt.[58] Conversely, if the plaintiff loses, usually after filing several appeals, there is very little recourse to seek compensation for the sacrifice of time spent and expenses incurred as a result of attorney's fees and court costs. This is even more demoralizing to the individual plaintiff than to its pharmaceutical counterpart because the latter can dig into its deep pockets and come out of such litigation essentially unscathed, aside from its attorney's fees and court costs.

Second, there may be criminal penalties. If the plaintiff can prove that the pharmaceutical company knew of the drug's safety defects and continued to market and sell it, the company and its principals may face criminal prosecution. Those within the company who knew of the drug's problems and failed to disclose such concerns may even face possible jail time. This may also result in class action lawsuits against the company and may lead to large fines from the FDA.

A. Vioxx Lawsuits: The Case Against Merck

In 2004, Vioxx was pulled off the market for safety reasons; at the time, Vioxx was the most profitable drug ever to be withdrawn from the market in United States history.[59] Merck withdrew Vioxx from the market after the data-

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Pill Linked to 63 Liver-Poisoning Deaths, CNN.COM, Mar. 23, 2000, http://archives.cnn.com /2000/HEALTH/03/22 /diabetes.drug.01/index.html. Bayer voluntarily withdrew Baycol from the market in 2001. David Brown, *Baycol Pulled from Market as Numerous Deaths Linked to It*, WASH. POST, Aug. 9, 2001, at A01.

[56] Some of the blockbuster drugs pulled off the market recently, such as Rezulin, Baycol, and Vioxx, treated disease-states such as diabetes, heart disease, and osteo-arthritis respectively.

[57] Rezulin and Baycol were manufactured by Pfizer and Bayer respectively.

[58] An example of a pharmaceutical global settlement occurred in November, 2001, when TAP Pharmaceuticals Inc. "agreed to pay a total of $875 million to resolve alleged violations of the Prescription Drug Marketing Act (PDMA) and criminal and civil allegations of fraudulent drug pricing and marketing conduct." Judith A. Waltz, *Multimillion Dollar Settlement Signals Government's Increased Scrutiny of Pharmaceutical Industry*, DRUG BENEFIT TRENDS, Nov. 2001, at 15-16, *available at* http://www.medscape.com/viewarticle/414901.

[59] *Vioxx Withdrawn After Study Suggests it May Double the Risk of Heart Attack*, SENIORJOURNAL.COM, Sept. 30, 2004, http://www.seniorjournal.com/NEWS/Health/4-09-

safety-monitoring board, which oversaw a long-term study of the drug, recommended that the study be halted.[60] In essence, patients in the study had an increased risk of developing serious cardiovascular events, such as heart attacks and strokes, because of their continued use of the Vioxx fifty milligram tablet, as compared to those patients simply taking a placebo.[61]

The FDA responded to Merck's stunning announcement by stating that "Merck did the right thing by promptly reporting these findings to the FDA and voluntarily withdrawing the product from the market."[62] The legal ramifications of such a withdrawal were unprecedented and over the next few weeks and months, injury lawyers across the country postured for position in an attempt to sue Merck and obtain a piece of the Vioxx injury pie.

The legal consequences of the Vioxx withdrawal were immense. In the United States alone 4,300 lawsuits were filed against Merck, citing Vioxx as the cause of an injury.[63] There may be several reasons why such a large number of lawsuits were filed. First, plaintiffs' attorneys targeted large pharmaceutical companies, and many of them used this opportunity to show prospective clients that trial lawyers can sue big conglomerates like Merck and hold them accountable.[64] Second, a significant number of the cases were to be tried in jurisdictions that fail to cap punitive damages.[65] As a result, plaintiffs' lawyers were hoping that the advent of big-ticket verdicts against the company would result in the filing of more lawsuits.[66] Similar to cases involving claims against asbestos and breast implants, plaintiffs' lawyers hoped that this marked the beginning of a long road of litigation.[67] Finally, a defeat in the courtroom might be the ultimate consequence of the withdrawal because it can lead to substantial jury awards and a considerable number of subsequent lawsuits.

Additionally, in 2005, three highly publicized Vioxx trials set the tone for

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30Vioxx.htm. Vioxx was a non-steroidal anti-inflammatory drug within the category of drugs known as cox-2 inhibitors. *Id.* It was prescribed by both specialists and general practitioners for pain associated with osteoarthritis. *Id.* Also, since Vioxx was marketed for the treatment of pain, many physicians prescribed it to octogenarians.

[60] *Id.*

[61] *Id.*

[62] *Id.* Acting FDA Commissioner Dr. Lester M. Crawford also stated that "[a]lthough the risk that an individual patient would have a heart attack or stroke related to Vioxx is very small, the study that was halted suggests that, overall, patients taking the drug chronically face twice the risk of a heart attack compared to patients receiving a placebo." *Id.*

[63] Anthony J. Sebok, *What's Next for Merck and its Lawyers? Vioxx Verdict Likely to Be Reduced But Could Impact Other Cases*, CNN.COM, Aug. 23, 2005, http://www.cnn.com/2005/LAW/08/23/sebok.vioxx/index.html.

[64] Sebok, *supra* note 63; JERRY AVORN, POWERFUL MEDICINES: THE BENEFITS, RISKS, AND COSTS OF PRESCRIPTION DRUGS 371 (2004).

[65] Sebok, *supra* note 63.

[66] *Id.*

[67] *Id.* A drawn out litigation process means that the company will likely settle, even those cases it might win, in an attempt to avoid a string of defeats that would provide other potential victims the incentive to sue. *Id.* It also could lead to forum shopping, resulting in adverse publicity for the company in multiple jurisdictions.

future litigation that would be sure to follow. Each of these trials presented a unique opportunity to examine the legal consequences of pulling a blockbuster drug off the market. So far there is no clear winner as the decisions sometimes favor Merck and other times favor the plaintiff.

The first trial occurred in the Texas case, *Ernst v. Merck*,[68] in which the widow of the decedent who used Vioxx for several months, claiming that Vioxx contributed to the decedent's death, sued Merck for negligence in the design of their blockbuster anti-arthritic drug.[69] The jury awarded a verdict in favor of the plaintiff for $253 million, including $229 million in punitive damages.[70] The jury determined that Merck acted with malice, which was defined as "an extreme degree of risk and conscious indifference to the rights, safety or welfare of others."[71]

This large award has several implications. First, as the largest award against a pharmaceutical company in U.S. history, it attracted hundreds of new lawsuits against Merck filed by plaintiffs' attorneys who wanted a piece of the pie. Second, the award sent a clear message to the pharmaceutical industry that pulling a blockbuster drug off the market could lead to crippling damage awards. Third, Merck was dealt a serious blow since this was only the first of thousands of lawsuits that it would face, and such a verdict and award set a very negative precedent. Finally, such a verdict not only encouraged plaintiffs to file more lawsuits, it also discouraged plaintiffs from settling their cases, hoping for a similar outcome by taking their cases to trial.

The second trial occurred in the New Jersey case, *Humeston v. Merck*,[72] and resulted in the pendulum swinging back in Merck's favor. This case proved that winning a lawsuit against a pharmaceutical company that has voluntarily withdrawn a blockbuster drug because of safety concerns is an unlikely proposition and is a great risk for the plaintiff.

In this case, even though the jury verdict was not permitted to address whether Vioxx caused a heart attack, the jurors had determined that other risk factors and job stress were contributing factors.[73] The jury determined that Merck provided adequate warning to prescribing physicians.[74] This verdict was a giant setback for many plaintiffs because it occurred in New Jersey, the loca-

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[68] *Texas Jury Awards $250 Million in 1st Vioxx Trial*, MEALEY'S PROD. LIAB. & RISK, Sept. 5, 2005, at 23, 23 [hereinafter *Texas Jury Awards $250 Million in 1st Vioxx Trial*].

[69] *Texas Jury Awards $250 Million in 1st Vioxx Trial, supra* note 68.

[70] Aaron Smith, *Jury: Merck Negligent: Merck Blamed for Death in Vioxx Suit; Jury Awards $253 Million in Damages. Drug Giant to Appeal.*, CNNMONEY.COM, Aug. 19, 2005, http://money.cnn.com/2005/08/19/news/fortune500/vioxx.

[71] *Texas Jury Awards $250 Million in 1st Vioxx Trial, supra* note 68.

[72] *New Jersey Jury Finds Vioxx Warnings Were Adequate*, MEALEY'S PROD. LIAB. & RISK, Dec. 2, 2005, at 29, 29 [hereinafter *New Jersey Jury Finds Vioxx Warnings Were Adequate*].

[73] *New Jersey Jury Finds Vioxx Warnings Were Adequate, supra* note 72.

[74] *Id.*

tion of Merck's corporate headquarters and the location of more than 2,700 other filed lawsuits.[75] Nevertheless, this victory proved that in any lawsuit against a major pharmaceutical company (with deep pockets and even deeper resources), wins and losses during the course of the litigation process depend on the facts as presented in individual cases.[76]

The third Vioxx trial and first federal trial, *Plunkett v. Merck*, took place in Houston, Texas, and resulted in a mistrial.[77] In *Plunkett*, the trial ended in a mistrial after the jury could not reach a conclusive verdict after nearly two and a half days of deliberation.[78] The judge stated that "the jury was split and unable to agree on a verdict."[79] Once again, the outcome of the trial rested on facts that ultimately left the jurors deadlocked.

The three Vioxx trials proved that pulling a blockbuster drug off the market can have significant and unpredictable legal consequences for both the plaintiff and the defendant. These trials also proved that extraneous factors can dictate the outcome of the trial. For instance, in all three trials, the facts played a critical role in swaying or deadlocking the respective juries.[80] In both the second and third trials, the individual facts of each case dictated the outcome in Merck's favor. In product liability cases, often the specific facts, such as the patient's administration of the pill or the patient's understanding of the prescribing information, can play a pivotal role in swaying the jury one way or another.[81]

Another critical factor in determining the outcome was the jurisdictional location of the lawsuit. For instance, the large award in the first trial was not unusual for Texas. Moreover, the second trial was held in New Jersey where Merck was incorporated; therefore, finding an unbiased jury may have proven difficult for the plaintiff. Finally, all three trials proved that a blockbuster drug being pulled off the market delineates the beginning of a long road of litigation for both parties. Thus, much like a boxing match, a resounding win in any one round can be easily reversed in subsequent rounds.

These three cases are only a small sample of the cases that Merck will face

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[75] *Id.*

[76] *Id.* At the time of the verdict in Merck's favor, there were 6,400 other lawsuits that had been filed against Merck. *Merck Acquitted in Second Vioxx Suit*, INJURY HELP LINE, Nov. 10, 2005, http://www.injuryhelpline.com/index.rwl?category=news&section=pharmaceutical&article=merck+acquitted+in+second+vioxx+suit&id=1901.

[77] *1st Federal Vioxx Trail Ends in Mistrial; Jury Split*, MEALEY'S PROD. LIAB. & RISK, Dec. 16, 2005, at 24, 24 [hereinafter *1st Federal Vioxx Trail Ends in Mistrial; Jury Split*].

[78] *Id.*

[79] *Id.*

[80] *Texas Jury Awards $250 Million in 1st Vioxx Trial*, *supra* note 68; *New Jersey Jury Finds Vioxx Warnings Were Adequate*, *supra* note 72; *1st Federal Vioxx Trail Ends in Mistrial; Jury Split*, *supra* note 77.

[81] It should be noted that this is not true in every case but seemed to matter in these early Vioxx cases.

in the next ten years.[82] These cases prove that the determining factors will be the merits of the respective case, the jurisdiction in which the case is tried, and the trial strategies employed by the parties. A resounding victory in one part of the country may be inconsequential to potential plaintiffs in other parts of the country. Nevertheless, the legal consequences can greatly affect all pharmaceutical companies and plaintiffs who use blockbuster drugs in the foreseeable future.

B. Criminal Indictments and Substantial Financial Penalties

A pharmaceutical company that pulls a blockbuster drug off the market either voluntarily or involuntarily is likely to receive major media attention. Most drugs are pulled off the market because there is indisputable evidence that the drug has caused health problems in those who used the drug. As a result, the next logical step is to question those involved in the development and manufacturing of the drug and to determine if such information could have been revealed earlier. Accordingly, if personnel within the pharmaceutical company had the information and failed to reveal its contents to the FDA or to decision makers within the company, not only is the company subject to civil lawsuits, but those who failed to disclose the information may be criminally prosecuted and the company may be penalized through large fines. In such a case, criminal indictments will probably be filed because of the potential severity of such a situation. It is inexcusable for a company to withhold information proving that a drug could be potentially harmful to those patients whom it is intended to benefit.

A little over a month after pulling Vioxx off the market, Merck revealed that it had been subpoenaed by the Justice Department concerning an investigation into the methods Merck had used to market and sell Vioxx.[83] In subsequent cases against Merck, plaintiffs' attorneys are likely to point to internal Merck memoranda that had at least three programs to train sales representatives "to misstate and misrepresent the truly dangerous nature of Vioxx to prescribing physicians," including a company document that alerted sales reps to dodge tough questions from physicians.[84] In addition, plaintiffs' attorneys will also use internal Merck e-mails and marketing materials as well as interviews with outside scientists to show that the company fought hard to keep safety concerns

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[82] There have been several cases following the initial three publicized cases. *See* Brooks v. Merck & Co. Inc., 443 F. Supp. 2d 994 (S.D. Ill. 2006); *see also* Melton v. Merck & Co. Inc, 2006 U.S. Dist. LEXIS 37376 (E.D. Ky. June 1, 2006); *see also* Salinas v. Merck & Co. Inc., 2006 U.S. Dist. LEXIS 12196 (S.D. Tex. Mar. 7, 2006).

[83] Amy Barrett, *Merck: How Much Misery After Vioxx? Bankruptcy Seems Unlikely, But Lawsuits Could Be a Drain for Years*, BUS. WK. ONLINE, Nov. 22, 2004, http://www.businessweek.com/magazine/content/04_47/b3909051_mz011.htm?chan=search.

[84] Cindi Solomon & Sandy Summers, *Vioxx: Birth and Death of a Super Aspirin*, 1-6 MEALEY'S LITIG. REP. ARTHRITIS DRUGS 15 (2004).

from destroying the drug's profit.[85] Furthermore, in 2005, The New England Journal of Medicine claimed that the authors of VIGOR, a landmark Vioxx clinical outcomes trial, erased data suggesting that three patients who took Vioxx in the trial suffered heart attacks.[86] Although there is mounting evidence that Merck employees knew about Vioxx's safety problems, the Justice Department has yet to file any criminal indictments against Merck.

In the past, a company's voluntary withdrawal of a blockbuster drug did not result in criminal indictments against decision makers within the company because in doing so the company conceded the drug's lack of safety and as a result attempted to rectify such a problem.[87] As more pharmaceutical companies require successful blockbuster drugs in order to offset the ever increasing research, development, and litigation costs, executives are faced with increasing pressure to circumvent any problems with potential blockbuster drugs that may arise. In doing so, it is likely that these executives might face criminal prosecution for attempting to hide concerns that might jeopardize the drug's commercial future.

Another consequence of concealing information that may reveal a blockbuster drug's safety problems is the imposition of substantial financial penalties on the pharmaceutical company that owns the drug. For instance, in 1996, Warner-Lambert Pharmaceuticals, before being acquired by Pfizer, submitted Rezulin, a drug aimed at treating patients with diabetes, to the FDA.[88] During the drug approval process, Warner-Lambert pressured the FDA into approving Rezulin, a drug with known side-effects, which were fatal in some cases.[89] This decision to approve the drug was ill-fated as the drug was allegedly related to the deaths of 391 people by the time it was pulled from the market.[90]

Prior to its submission of Rezulin to the FDA, Warner-Lambert was already being investigated by the FDA and the Justice Department for its concealment of key information and actions during the drug approval process.[91] Eventually, Warner-Lambert pled guilty in 1995 for "concealing quality-control problems in its drug manufacturing" processes and received a ten million dollar

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[85] Alex Berenson, *In Training Video, Merck Said Vioxx Did Not Increase Risk of Heart Attack*, N.Y. TIMES, July 21, 2005, at C4, *available at* http://www.vioxx-recall-lawsuit.com/news/video.pdf.

[86] Chris Rangel, *Unprecedented! The New England Journal Accuses Vioxx Study Authors of Cover-Up!*, RANGELMD.COM, Dec. 9, 2005, http://www.rangelmd.com/2005/12/new-england-journal-fingers-vioxx.html.

[87] A company can rectify such a problem by further testing the drug or settling lawsuits with any adverse party.

[88] Melissa Marie Bean, *Fatal Flaws in the Food and Drug Administration's Drug-Approval Formula*, 2003 UTAH L. REV. 881, 904, 908 (2003). Rezulin was approved to lower blood sugar, which is critically important to diabetic patients because it helps the body process insulin. *Id.* at 903.

[89] *Id.* at 904-05.

[90] *Id.* at 903.

[91] *Id.* at 904.

fine; at the time, this was one of the largest fines ever imposed on a drug manufacturer.[92] Although that number may not seem significant for a large pharmaceutical conglomerate with deep pockets, the fine represented the determination by governmental agencies that the pharmaceutical company erred in its manufacturing of the drug. In turn, such a finding could be used by plaintiffs' attorneys in subsequent civil lawsuits.

V. BUSINESS RAMIFICATIONS OF PULLING A DRUG OFF THE MARKET

In addition to legal consequences, such as civil lawsuits and criminal indictments, a pharmaceutical company can also face business consequences as a result of a blockbuster drug withdrawal from the market. One of these consequences is the loss of an asset that produces a significant amount of revenue for the company. Another is the myriad of lawsuits and the significant amount of capital required for their defense. Also, the company can face a decrease in the market's valuation of the company, specifically in its stock price, which can affect perception and investor confidence in the company's ability to bounce back from such a setback. Nevertheless, regardless of the reason, the loss in profit and future revenues can be devastating for any company, especially if the drug is a significant asset within its product line.

Bayer Pharmaceuticals faced the business ramifications of pulling a blockbuster drug off the market when, in 2001, it pulled Baycol,[93] one of its most profitable pharmaceutical drugs used to treat high cholesterol, off the market. As a result, Bayer had to prepare itself for the long road of litigation by stockpiling a significant amount of capital to fight lawsuits.[94] Unlike its statin counterparts, Zocor, Lipitor and Pravacol, Bayer's Baycol was related to the deaths of nearly one hundred people and was associated with causing painful side effects, such as rhabdomyolosis, which causes weakening of the muscles.[95] Since its withdrawal, many plaintiffs' attorneys had been critical of Bayer's handling of the drug, even claiming that Bayer's litigation costs (due to the withdrawal of Baycol) would ultimately cost fifty billion dollars in settlements and judgments before it was over.[96]

As a result of the negative press it received and the numerous lawsuits that were filed against it, Bayer faced a significant financial setback due to Baycol's withdrawal. At first, Bayer settled 2,312 cases for $872 million, including several settlements of one million dollars for the roughly 100 death cases.[97] In or-

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[92] *Id.*

[93] Baycol was a cholesterol lowering drug within the category of drugs known as statins.

[94] Monica Langley, *Bayer, Pressed to Settle a Flood of Suits Over Drug, Fights Back*, WALL ST. J., May 4, 2004, at A1, *available at* http://webreprints.djreprints.com/1220931162452.html.

[95] *Id.*

[96] *Id.*

[97] *Id.*

der to cover the legal costs associated with the nearly 9,278 lawsuits pending since Baycol was pulled from the market, Bayer set aside nearly $1.2 billion, mostly provided by insurers.[98] Furthermore, Bayer had to plan for any possible losses in such cases or in settlement of some of the lawsuits. From its initial withdrawal of Baycol until 2004, Bayer had settled 2,312 lawsuits and as a result paid nearly $872 million.[99] There were over 9,000 lawsuits pending, which plaintiffs' attorneys, such as Mikal Watts, believe will end up costing the company in excess of fifty billion dollars.[100] Therefore, not only did Bayer lose one of its most profitable products, but it was faced with the prospect of using capital that it had reserved for research and development of other compounds to fend off plaintiffs' attorneys who wanted a piece of the ever-increasing lawsuit pie.

Another possible financial consequence of pulling a drug off the market is the stock market's downward valuation of the company in terms of its stock price. In Bayer's case, as a result of the thousands of lawsuits that had been filed against the company and the long road of litigation ahead which the company would inevitably have to face over the next decade, the company saw a significant setback in its stock price.[101] The lack of market confidence in Bayer remained even though Bayer produced several high profile blockbuster drugs after Baycol's withdrawal, including Levitra, a drug used to treat erectile dysfunction.

Another example of a company's stock devaluation due to a drug withdrawal occurred when Merck voluntarily withdrew Vioxx from the market. Arguably, no pharmaceutical company has faced Wall Street's wrath quite like Merck, which faced a significant decrease in stock price after pulling Vioxx off the market because of impending litigation.[102] It is easy to see how investor faith in the pharmaceutical industry has begun to wane as a result of continual litigation[103] and the fact that Vioxx was the ninth prescription drug to be involuntarily withdrawn from the market due to death or injury in the last seven years.[104] Also, Vioxx was a different type of blockbuster drug: Vioxx was a

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[98] *Id.*

[99] *Id.*

[100] *Id.*.

[101] Yahoo! Finance, Bayer Historical Prices, Date Range: Nov. 18, 2000 to Jan. 4, 2003, http://finance.yahoo.com/q/hp?s=BAY&a=10&b=18&c=2000&d=00&e=4&f=2003&g=m (last visited Feb. 20, 2007). From 2001 to 2003, Bayer's stock price decreased by approximately eighteen dollars, in large part due to the damage caused by the withdrawal of Baycol from the market and a lack of confidence from investors that the company would bounce back in the wake of impending litigation.

[102] Yahoo! Finance, Merck Historical Prices, Date Range: Aug. 2, 2004 to Nov. 4, 2004, http://finance.yahoo.com/q/hp?s=MRK&a=07&b=2&c=2004&d=10&e=4&f=2004&g=d (last visited Feb. 20, 2007). In a span of three months, from August 2004 to October 2004, Merck's stock price dropped by approximately sixteen dollars due to the voluntary withdrawal of Vioxx.

[103] *Id.*

[104] Placitella & Klein, *supra* note 33, at 222.

veritable super blockbuster drug, if such a term exists. It had entered the market to much hype in 1999 and became an instant success, grossing over one hundred million prescriptions, including twenty million users, and about $2.5 billion in annual sales.[105] The fact that Vioxx was such a highly advertised drug led to a firestorm of publicity and made it all the more vulnerable to individual plaintiff and class action lawsuits, such as personal injury tort actions, derivative lawsuits, congressional investigations, and Securities and Exchange Commission inquiries.[106]

Subsequently, on the day Vioxx's withdrawal was announced, Merck shares lost more than twelve dollars per share, dropping from forty-five to thirty-three dollars per share, later stabilizing to around thirty dollars per share.[107] The withdrawal of Vioxx also caused Merck, the nation's third largest pharmaceutical company, to be thought of as a potential merger target.[108] In fact, in the months to follow, Merck's Board of Directors offered special bonuses to 230 of its most senior managers, which would be triggered if either the company was taken over by another firm or if some other firm acquired twenty percent of its outstanding shares.[109]

The Vioxx episode proved that not only is the pharmaceutical company susceptible to a drop in stock price, but as a result, the company may also face a hostile takeover by another company, greatly affecting investor confidence in the company. Nevertheless, any company that wished to take over Merck would also have to take on the thousands of lawsuits that Merck faced as a result of Vioxx's withdrawal.

Furthermore, Vioxx's withdrawal cost many Merck employees their jobs. Since the withdrawal, Merck has planned to layoff nearly 7,000 employees, most of whom held production plant jobs.[110] In addition, top executives are not often spared after a major drug withdrawal. For instance, Merck's Chairman and Chief Executive Officer, Raymond Gilmartin, abruptly resigned shortly after Vioxx was withdrawn from the U.S. market.[111] Therefore, the business

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[105] Richard A. Epstein, *Regulatory Paternalism in the Market for Drugs: Lessons from Vioxx and Celebrex*, 5 YALE J. HEALTH POL'Y L. & ETHICS 741, 741 (2005).

[106] *Id.* at 742; *see also Congressional Hearing Focuses on Merck's Marketing for COX-2 Drug Vioxx*, THE KAISER FAMILY FOUND. DAILY REPORTS, May 6, 2005, http://www.kaisernetwork.org/daily_reports/rep_index.cfm?hint=3&DR_ID=29882.

[107] Epstein, *supra* note 105, at 743; *see also* Aaron Smith, *Canadian Vioxx Study Challenges Merck: Vioxx Increases Heart Attack Risk in First Few Weeks of Use, Study Says; Merck Dismisses Findings.*, CNNMONEY.COM, May 3, 2006, http://money.cnn.com/ 2006/05/03/news /companies/vioxx/index.htm.

[108] Epstein, *supra* note 105, at 743.

[109] *Id.*

[110] Joseph Kay, *Merck Announces 7,000 Layoffs – Continued Attack on Jobs and Wages in US*, WORLD SOCIALIST WEB SITE, Dec. 2, 2005, http://www.wsws.org/articles/2005/dec2005/jobs-d02.shtml.

[111] Phil Taylor, *Manufacturing Head Takes Merck Top Spot as Gilmartin Quits*, DRUGRESEARCHER.COM, Sept. 5, 2005, http://www.drugresearcher.com/news/ng .asp?n=59844-

ramifications of pulling a drug from the market can affect all of a company's divisions, from the boardroom to the factory floor.

Finally, it should be noted that once the patent on a blockbuster drug expires, other companies can use the same drug's formula to create generic drugs. The proliferation of generic drugs often cannibalizes the market for the original blockbuster drug. Therefore, for pharmaceutical companies that possess multiple blockbuster drugs, one of the drugs whose patent may be close to its expiration, a drug withdrawal of the other drug or drugs may be financially crippling. As a result, this may lead to increasing motivation on the part of the respective pharmaceutical company to produce more blockbuster drugs in order to make up for the loss of these profitable assets.[112]

VI. ETHICAL CONSIDERATIONS OF PULLING A DRUG OFF THE MARKET

The decision to withdraw a blockbuster drug from the market can present ethical dilemmas to the following parties: the pharmaceutical company, the regulatory agencies, such as the FDA, and the pharmaceutical industry as a whole. For instance, before pursuing a withdrawal, the pharmaceutical company must take into account that there are patients who may be dependent on these arguably life altering drugs, such as Vioxx and Lipitor.[113] In addition, the pharmaceutical industry is forced to consider that many patients are "counting on industry research to produce new treatments for diseases like rheumatoid arthritis and diabetes."[114] Finally, regulatory agencies such as the FDA have begun to carefully scrutinize ethical considerations because "nobody wants to be on 60 Minutes being asked why a dangerous drug was approved" and whether the FDA took into account that countless Americans that would be negatively affected due to side effects and many more would be left without a viable alternative once that drug was withdrawn from the market.[115]

Subsequently, all of the players in this drama have begun to take into consideration how a drug withdrawal may affect not just their respective entities, but also the lives of many patients. The most prominent player in this drama, however, is the pharmaceutical company, and although the FDA and the pharmaceutical industry also face certain ethical issues, most of these issues are a by-product of those faced by the pharmaceutical company. As a result, for the purposes of this Note, the pharmaceutical company's ethical considerations or lack thereof will be examined and scrutinized.

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manufacturing-head-takes.

[112] Greg Radinsky, *The Spotlight on PBMs: Federal Enforcement of the Anti-Kickback Statute on the Pharmaceutical Benefit Management Industry*, 2 J. HEALTH L. 213 (2003).

[113] Alex Berenson, *Big Drug Makers See Sales Erode with Their Image*, N.Y. TIMES, Nov. 14, 2005, at A1.

[114] *Id.*

[115] *Id.*

A. Ethical Considerations Faced by the Pharmaceutical Company Before and After Drug Withdrawal

Although a withdrawal might be in the best interests of the pharmaceutical company, it is often not in the best interests of the patients who use the drug and are dependent on it for their daily activities. Therefore, this section of the Note will examine the ethical considerations that a pharmaceutical company must undertake before and after a drug withdrawal.[116]

Obviously from the perspective of a pharmaceutical company, a drug withdrawal is not an ideal solution because it leads to negative public perception, strained investor relations, and loss of a valuable asset.[117] In short, there are rarely any positive aspects to a drug withdrawal. Before a drug withdrawal has transpired, however, it is important for a pharmaceutical company to note that it can minimize the negative aspects of a drug withdrawal with a proper handling of the situation. Therefore, a pharmaceutical company's evaluation of the ethical considerations before a drug withdrawal may mitigate the negative public perception and strained investor relationship it is sure to face.

The stakes for all involved in a drug withdrawal, whether voluntary or involuntary, are enormous. As a result, before a decision is made as to whether a blockbuster drug will be withdrawn from the market, the respective pharmaceutical company must evaluate how such an announcement will affect the countless number of patients who are counting on the drug to treat a life-altering ailment. In addition, such an announcement also forces health care professionals to face the prospect of finding alternative forms of relief for patients who can no longer use the withdrawn blockbuster drug. In the case of voluntary withdrawal, the pharmaceutical company can balance such ethical considerations with the fact that they must ensure the safety of the general public. Also, the company can fall back on the fact that it took all the necessary precautions, such as adding warning labels as required by the FDA, but in such a case, the risk outweighed any potential benefit that the blockbuster drug provided.[118]

Conversely, the pharmaceutical company is faced with the prospect of continuing to market and manufacture a defective product, particularly, one that posed a danger to those patients who used it. In addition, the pharmaceutical company also must consider the ethics of continuing to market a product whose failures are delineated in clinical outcomes studies. As a result, the pharmaceutical company's failure to act may have led to countless more deaths that may have been avoided through both the drug's withdrawal from the market and timely notice of the drug's withdrawal to physicians and patients.[119] Therefore,

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[116] Epstein, *supra* note 105, at 745.

[117] Aaron Smith, *Drug Company Could Use a Face Lift*, CNNMONEY.COM, Aug. 19, 2005, http://money.cnn.com/2005/08/16/news/fortune500/drugindustry/index.htm?section=money_latest.

[118] *Id.*

[119] *See* Bean, *supra* note 88.

a failure to take into account these important ethical considerations can lead to devastating consequences including a FDA mandated withdrawal, negative public perception, and strained investor relationships.

Every pharmaceutical company must balance the benefits of producing a blockbuster drug with the risk of loss of life or serious injury that may result due to an adverse event or other usage problem. In addition, every pharmaceutical company, through their membership in PhRMA, understands that they have an important duty to treat patients on their road to recovery.[120] Nevertheless, given the ethical duties voluntarily undertaken by the pharmaceutical industry and its companies, pharmaceutical companies are continually faced with accusations from the public, government officials, and regulatory officials that they failed to take into account the ethical consideration of continuing to manufacture a drug whose safety problems were readily ascertained from ongoing clinical-outcomes studies.[121]

In addition, although in recent years, pharmaceutical companies have been forced to withdraw an increasing number of blockbuster drugs, many of these drugs have been withdrawn after a significant number of patient deaths. For instance, from 1997 until 2001, thirteen drugs were pulled off the market, having been linked to consumer deaths and severe side effects.[122] Several of these thirteen drugs were on the market for many years before they were withdrawn, begging the question whether the respective pharmaceutical company should have been allowed to wait for evidence of the drugs' safety problems to accumulate before finally being forced to withdraw the drug, especially in light of their ethical obligation to improve patients' well-being.[123]

A more recent example of a pharmaceutical company's alleged failure to withdraw a drug from the market despite the proof of its safety problems was the Vioxx drug withdrawal. Several notable medical journals, including *The*

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[120] Pharmaceutical Research & Manufacturers of Am., About PhRMA, http://www.phrma.org/about_phrma/ (last visited Feb. 20, 2007). PhRMA is an association of pharmaceutical companies that helps regulate the pharmaceutical industry. *Id.* "PhRMA's mission is winning advocacy for public policies that encourage the discovery of life-saving and life enhancing new medicines for patients by pharmaceutical/biotechnology research companies." Pharmaceutical Research & Manufacturers of Am., Mission Statement, http://www.phrma.org/mission_statement/.

[121] *The Baycol/Lipobay – Scandal: First Trial Set to Start for Bayer's Baycol*, DR- RATH-FOUNDATION.ORG, Feb. 18, 2003, http://www4.dr-rath-foundation.org/PHARMACEUTICAL_BUSINESS/ BAYCOL/baycol08.htm. The Dr. Rath Health Foundation is a leading website providing information on natural health. *Id.* During a trial against Bayer, the plaintiff attempted to show that "Bayer withheld from the FDA negative results of Baycol's clinical trials." *Id.*

[122] *Safety-Based Drug Withdrawals (1997-2001)*, FDA CONSUMER MAG., Jan.-Feb. 2002, *available at* http://www.fda.gov/fdac/features/2002/chrtWithdrawals.html. The thirteen withdrawn drugs include Baycol, Raplon, Lotronex, Propulsid, Phenylprpanolamine, Rezulin, Hismanal, Raxar, Posicor, Duract, Seldane and Seldane-D, Pondimin, and Redux. *Id.*

[123] *Id.*

Lancet,[124] criticized Merck's handling of the Vioxx situation, specifically, its failure to withdraw the drug when the existence of safety issues became obvious.[125] During the Vioxx Senate Hearings months after the withdrawal, Associate Director for Science and Medicine in the FDA's Office of Drug Safety, Doctor David Graham, "explained that Vioxx is a prime example of the national tragedy that occurs when the FDA and the manufacturer" do not take into consideration the effect a failure to withdraw the drug might have on prospective and current patients.[126] He stated that, "Vioxx 'may be the single greatest drug safety catastrophe in the history of this country' that 'largely could have been avoided but wasn't.'"[127] Furthermore, "Doctor Graham estimated that 88,000 to 139,000 Americans were injured by Vioxx" and that thirty to forty percent of them probably died, analogizing the magnitude of the harm to "the rough equivalent of 500 to 900 aircraft [sic] dropping from the sky."[128] Many prominent members of the medical community agreed with Doctor Graham that countless deaths and much suffering could have been avoided had Vioxx been recalled four years earlier. This opinion was supported by an editorial appearing in the *The Lancet*.[129] In the article, the author commented that both "Merck and the FDA acted out of ruthless, short-sighted, and irresponsible self-interest."[130]

Merck was not the only pharmaceutical company in recent years that failed to take into account the ethical ramifications of pulling a drug off the

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[124] The Lancet is a medical journal originally founded in 1823. TheLancet.com, About The Lancet, http://www.thelancet.com/about (last visited Feb. 20, 2007). It publishes clinical trials and opinions of notable health care professionals. *Id.* It claims not to be affiliated with any medical organization. *Id.*

[125] Tom Armitage, *Merck Should Have Pulled Vioxx in 2000 – Study*, REUTERS, Nov. 4, 2004, *available at* http://www.lexisnexis.com (click on News and Business, click on Individual Publications, click on R, click on Reuters News) (arguing that Merck executives should have withdrawn Vioxx from the market in 2000 while citing a report in the British medical journal, "The Lancet". In that report, "researchers at the University of Berne said there was substantial evidence of the dangerous side effects of the drug by the end of 2000, but the mounting data was not analyzed properly"); *see also* Richard Horton, *Vioxx, The Implosion of Merck, and Aftershocks at the FDA*, 364 THE LANCET 1995, 1995-1996 (2004) (citing a cumulative meta-analysis showing the cardiovascular risks of Vioxx as early as 2000); *contra* Peter S. Kim & Alise S. Reicin, *Discontinuation of Vioxx*, 365 THE LANCET 23, 23 (2004) (arguing analyses by Juni and Horton of past Vioxx meta-analyses reached flawed conclusions).

[126] Placitella & Klein, *supra* note 33, at 221; *see also* Testimony of David J. Graham, MD, MPH: November 18, 2004, *available at* http://www.mercola.com/2005/mar/2/david_graham_testimonial.htm, *cited in* Joseph Mercola, *Vioxx Reapproved by FDA Panel Members With Ties to Drug Companies*, eHEALTHY NEWS YOU CAN USE, Mar. 2, 2005, http://www.mercola.com/2005/mar/2/vioxx_fda.htm.

[127] Placitella & Klein, *supra* note 33, at 221.

[128] *Id.*

[129] Mike Adams, *Reputation of the FDA in Shambles After Vioxx Scandal; Calls for Wholesale FDA Reform Gain Momentum*, NEWSTARGET.COM, Nov. 6, 2004, http://www.newstarget.com/002157.html.

[130] *Id.*

market. In 2001, Baycol was withdrawn from the market, but only after it had been linked to thirty-one deaths.[131] Bayer claimed that the drug was safe, but "[t]he industry's focus on producing drugs for chronic conditions like depression and diabetes has vastly increased the pool of potential plaintiffs, because medicines for those diseases are taken by millions of people."[132] Moreover, "because clinical trials for new drugs are conducted on only a few thousand subjects, the tests do not always discover . . . dangerous side effects."[133]

Bayer's argument can be criticized for several reasons. First, more testing should have been performed, especially when the drug is being mass produced and marketed to a wide number of patients and physicians.[134] Second, the drug was withdrawn after thirty people died during post-marketing surveillance, a number that seems much too high given the fact that this drug was used to prevent heart attacks and strokes.[135] In sum, more consideration should have been given to the fact that the drug was not properly tested and could negatively affect many of the patients for whom it was prescribed.

B. A Blockbuster Drug's Withdrawal May Affect Those Patients Who Have Not Reacted Negatively to the Drug

Another ethical consideration that a pharmaceutical company must consider when deciding whether to withdraw a blockbuster drug from the market is how such a withdrawal will affect current patients.[136] Many patients depend on drugs such as Vioxx and Bextra, not only for their pain relief properties, but also because these drugs give patients the ability to perform activities that otherwise would not be possible without pain.[137] As a result, due to the withdrawal, these patients are not afforded the chance to determine whether continued use of the withdrawn drug and any possible associated health risks

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[131] Posting of Louise McKichan, Baycol Killed 140 People Taking Its Statin, to http://www.rxlist.com/rxboard/pravachol.pl?read=143 (Feb. 26, 2005, 15:28 EST).

[132] Alex Berenson, *Trial Lawyers Now Take Aim at Drug Makers*, N.Y. TIMES, May 18, 2003, at A6.

[133] *Id.*

[134] *See* Ben Harder, *Dangerous Practices: Critics See Flaws in Drug-Safety Monitoring*, SCI. NEWS ONLINE, Feb. 5, 2005, http://www.sciencenews.org/articles/ 20050205/bob10.asp. Critics of Bayer claim that the company had become aware of the hazards even as it continued to sell Baycol and that it imperiled its customers by choosing not to disclose those risks fully. Several thousand lawsuits have been brought against the company. Four researchers who were paid by prosecutors to testify as expert witnesses studied the medical literature and internal company documents that were made public during the legal proceedings. Reporting in the same issue of JAMA in which Graham's report appears, they conclude that the data Bayer released while marketing Baycol did not tell the whole truth about the drug. *Id.*

[135] *Id.*

[136] *See* Julie Appleby & Anita Manning, *For Those in Pain, Relief Trumps Risks of Banned Painkillers*, USA TODAY, Jan. 4, 2005, at 1A, *available at* http://www.usatoday.com/news/ health/2005-01-04-painkillers_x.htm.

[137] *See id.*

may be worth the risk, given the very real possibility that without these drugs, their quality of life would be substantially diminished. [138]

Subsequently, without these drugs many patients are forced to use substitute drugs that are often not as efficacious or potent.[139] In some cases, the substitute drugs can also cause distress and side effects.[140] For instance, with the withdrawal of Vioxx and Bextra, many patients were forced to use over-the-counter drugs such as Advil and Aleve, both of which can also cause cardiovascular problems and digestive distress, although at a much lower rate than the cox-2 inhibitors.[141] Furthermore, withdrawal of many of the blockbuster drugs does not affect all patients negatively, causing many patients to wonder why they have been deprived of effective treatment. In most drug withdrawal cases, the vast majority of patients are not at risk for any of the side effects listed.[142] In fact, an FDA advisory panel even concluded that Vioxx was safe enough to be returned to the market as long as patients were better warned of the risks.[143] Furthermore, these patients might actually be more at risk from substitute drugs than from the withdrawn drugs. Therefore, many patients are left to wonder

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[138] *See id.*; *see also Life Without Vioxx: What's a Patient to Do?*, CONSUMERAFFAIRS.COM, Oct. 1, 2004, http://www.consumeraffairs.com/news04/vioxx_alternatives.html.

[139] *See Life Without Vioxx: What's a Patient to Do?, supra* note 138.

[140] Mayo Clinic Staff, NSAIDS: How to Avoid Side Effects, Apr. 3, 2006 [hereinafter NSAIDS: How to Avoid Side Effects] (on file with author). Aspirin and Advil are categorized as Non-Steroidal Anti-Inflammatory Drugs ("NSAIDs"), which are known to cause stomach ulcers and other gastrointestinal side effects. *See* MayoClinic.com, Anti-Inflammatory Drugs, Nonsteroidal (Systemic), http://www.mayoclinic.com/health/drug-information/DR202743 (last visited Feb. 24, 2007). Other classes of NSAIDs can also cause cardiovascular problems. NSAIDS: How to Avoid Side Effects, *supra*.

[141] *See Life Without Vioxx: What's a Patient to Do?, supra* note 138.

[142] *See* PainConcern.com, How Safe Are My Pills?, Mar. 3, 2005, http://www.painconcern.org.uk/pages/page62.php. In a recent study, the United States Food and Drug Administration ("FDA") examined heart attack risk in patients who used Vioxx. *Id.* The FDA studied a total of 1.4 million Californians who were using painkillers, including 1,000,000 patients who were using ibuprofen, 400,000 using naproxen, 40,000 using Celecoxib, and 27,000 using Vioxx. *Id.* Additionally, among the 1.4 million patients, the total number with coronary heart disease was 8,100. *Id.* "[B]ut when the incidence of coronary heart disease was compared with individual drugs they found a 1.6x higher risk, i.e. 1% in patients using Vioxx. So if you are a doctor in California and you have 1000 patients on painkillers other than Vioxx, you might find that 6 of them have coronary heart disease. And if you have 1000 patients on Vioxx you might find that 10 have heart disease. That's the problem. How do you decide if such a small increase is chance or genuinely due to the drug?" *Id.*

[143] *FDA Panel Concludes Vioxx Safe Enough to Return to Market*, NEWSTARGET.COM, Feb. 28, 2005, http://www.newstarget.com/005033.html; *Vioxx Could Be Sold Again*, MEALEY'S LITIG. REP. ARTHRITIS DRUGS, Feb. 1, 2005, at 8, 11 [hereinafter *Vioxx Could Be Sold Again*]. With the approval of a closely divided joint advisory committee of the FDA that also voted to keep competitors Celebrex and Bextra available, Vioxx could re-enter the pharmaceutical marketplace. A joint committee of thirty-two experts convened by the FDA voted 17-15 on Feb. 18, 2005, that Vioxx should be permitted back on the market. The committee voted 31-1 in favor of Celebrex and 17-13 with two abstentions for Bextra. *Vioxx Could Be Sold Again, supra.*

whether the chances of being harmed by a side effect of a withdrawn drug outweigh the increased quality of life associated with using the withdrawn blockbuster drug.[144]

C. Balancing Ethical Considerations with the Company's Stated Goal of Profitability

Most pharmaceutical companies must consider the ethics of putting profits before patient safety. In the 1950s, Merck patriarch and President George Merck remarked, "medicine is for the people. It is not for profits."[145] In recent months, his company has been criticized for hiding the problems associated with Vioxx in order to increase profits.[146] Although such allegations have not been substantially proven, companies that fail to consider the plight of patients and their families are likely to suffer from negative public perception that may affect the company for years to follow. In addition, such companies would likely face endless litigation and claims of negligence, which could continue for a seemingly indefinite period of time.

When making the decision to withdraw a drug from the market, a pharmaceutical company must first consider the patient. Often, a company is forced to confront the families of the patients who died or were injured as a result of using the blockbuster drug in question. But the company must also consider the plight of those patients who have not experienced side effects in connection with use of the drug. Such patients may be harmed as a result of the drug being withdrawn from the market, particularly if there is a lack of efficacious substitutes. Therefore, the ethical ramifications of withdrawing a blockbuster drug from the market are numerous and affect all parties involved.

VII. CONSIDERATIONS OF CULPABILITY IN PULLING A DRUG OFF THE MARKET

The question of who is at fault when a drug is withdrawn from the market is not easily discernible, even though the parties who are responsible can be easily identified. Most of the time, the party held responsible is the most visible party, usually the pharmaceutical company that developed and marketed the failed product. Pharmaceutical companies, however, are large conglomerates with multi-tiered management committees and divisions. As a result, assigning the blame to a particular individual or division of the com-

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[144] *See Vioxx Could Be Sold Again*, *supra* note 143.

[145] Raymond V. Gilmartin, Chairman, President, and Chief Executive Officer, Merck & Co. Inc., *Remarks of Raymond V. Gilmartin, Chairman, President, and Chief Executive Officer, Merck & Co., Inc. at Town Hall Los Angeles*, July 29, 2004, *available at* http://www.merck.com/newsroom/executive_speeches/072904.html.

[146] *See Medical Journal Revelation That Study Omitted 3 Deaths Prompts Call for Mistrial*, MEALEY'S LITIG. REP. ARTHRITIS DRUGS, Dec. 1, 2005, at 5, 6.

pany can be almost impossible and requires proof that certain individuals had knowledge of the drug's safety failures and subsequently failed to report them.

A. To What Extent is the Pharmaceutical Company at Fault?

The proof required to hold a pharmaceutical company liable for marketing and distributing an unsafe product is difficult to produce. After a drug has been pulled off the market, both the FDA and the respective pharmaceutical company incur significant expenses in order to investigate how such a safety failure transpired. Such investigations can take years and may cost millions of dollars; nonetheless, they produce valuable evidence-based answers regarding the drug's failure. Any information regarding management malfeasance and a failure to report important safety information is not easily discoverable. Therefore, even though a pharmaceutical company may be held liable for continuing to mass market and produce an unsafe product, it may escape any punitive liability because the opposing party will likely be unable to produce sufficient proof that the pharmaceutical company's management knowingly and intentionally produced the harmful drug.

Moreover, pharmaceutical companies argue that it is difficult to predict how a patient will react to a drug after years of concomitant treatment with other drugs. For instance, most drugs are tested under rigid clinical conditions. When placed on the market, however, a patient may fail to read the prescribing information circular[147] carefully. Often times, patients ingest a drug concurrently with other substances, such as food, drinks, or other drugs, which is strictly forbidden in the drug's prescribing information. In addition, most drugs have long half-lives.[148] As a result, a drug can be present in a patient's body for many years.[149] Because of this, it is difficult to assess the long-term effects of the drug because the drug usually is not tested for that length of time during

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[147] A prescribing information circular is a sheet of paper that is included when a drug is prescribed to a patient and is required to contain, among other requirements, "a summary of the essential scientific information" and comprehensive prescribing information. Labeling Requirements for Prescription Drugs and/or Insulin, 21 C.F.R. §§ 201.56 to 201.57 (2006). It also provides the patient with other information, such as concomitant use and the drug's mechanism of action. *Id.* § 201.57. It is "also referred to as a package insert, product label, or product information." HepititisBHelp.com, Glossary, http://www.hepatitisbhelp.com/hepatitis_b_glossary.html (last visited Feb. 24, 2007).

[148] Answers.com, Dictionary, half-life, http://www.answers.com/topic/half-life (last visited Feb. 24, 2007). The half-life of a substance subject to exponential decay is "[t]he time required for half of the quantity of a drug . . .to be metabolized or eliminated by normal biological processes." *Id.*

[149] *See, e.g.*, Julienne K. Kirk & John G. Spangler, *Alendronate: A Bisphosphonate for Treatment of Osteoporosis*, AM. FAMILY PHYSICIAN, Nov. 1, 1996, *available at* http://www.findarticles.com/p/articles/mi_m3225/is_n6_v54/ai_18890140. For instance, the terminal half-life of Fosamax, a drug that helps treat osteoporosis in men and women, is estimated to exceed ten years. *Id.*

clinical trials. Moreover, pharmaceutical company proponents argue that it is unrealistic to expect a drug to be tested for every possible side effect and adverse event because there are too many different scenarios under which a drug may be ingested by the average patient. Furthermore, each patient's body reacts differently to a drug; an adverse event in one patient may not be found in another. Nevertheless, most litigation is still directed towards the pharmaceutical company when a drug is withdrawn from the market because it is the party that marketed and distributed the failed product. Thus, it can be argued that just as a pharmaceutical company takes credit for a successful novel medicine and as a result reaps the financial rewards, it must also be held accountable and publicly responsible for developing and marketing an unsafe drug in order to prevent companies from submitting drugs to the market that have not been thoroughly tested.

B. To What Extent is the FDA at Fault?

Another visible party who does not escape liability for its failure to adequately monitor the safety issues associated with a withdrawn drug is the FDA. Often times, medical experts and insiders within the FDA will publicly ridicule the FDA for a lack of sustained scrutiny of certain pharmaceutical drugs after these drugs have been approved for sale and distribution in the U.S. market. For instance, during the very public Vioxx Senate Hearings, Doctor David Graham testified that the FDA failed in its attempt to protect the American consumer from unsafe drugs and that as a result, thousands of Americans suffered cardiovascular events that may have been avoided.[150] Other experts have also testified that the FDA has pandered to the interests of the "Big Pharma" and as a result has failed to objectively regulate the introduction of new drugs on the market.[151] This kind of public ridicule and testimony by respected members of the medical profession is extremely damaging, especially to a regulatory agency charged with protecting U.S. citizens from harmful products, and it could lead to future congressional action and examination into drug approval practices.[152]

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[150] *See* Risa L. Lieberwitz, *Education Law: The Corporatization of Academic Research: Whose Interests Are Served?*, 38 AKRON L. REV. 759, 768 (2005); *see also* Lisa Richwine, *FDA Failed Public on Vioxx*, REUTERS, Nov. 18, 2004, *available at* http://www.lexisnexis.com (click on News and Business, click on Individual Publications, click on R, click on Reuters News).

[151] Lieberwitz, *supra* note 150, at 768-69. During the Vioxx House Committee Hearings, Minnesota Congressman Gil Gutknecht commented, "[j]ust who is the FDA protecting, and what are the ethical responsibilities of pharmaceutical companies? Both the FDA and the pharmaceutical company sort of missed the mark." Bernadette Tansey, *Vioxx: How Marketing Drives the Pharmaceutical Industry: Firm Misled Doctors on Vioxx, Panel Says Sales Staff Told Not to Discuss Risk Study*, S. F. CHRONICLE, May 6, 2005, at A1.

[152] *See Evaluating the Effectiveness of the Food and Drug Admin. Modernization Act Before the Subcomm. on Health of the H. Comm. on Energy and Commerce*, 107th Cong. 51, at 16-17 (2001) (statement of W.J. "Billy" Tauzin, Chairman, Committee on Energy and Commerce). Tauzin, the Chairman of the Committee on Energy and Commerce, was optimistic

C. To What Extent is the Health Care Professional at Fault?

While the pharmaceutical company and the FDA share the brunt of the blame, in some cases, other smaller groups are also blamed for failing to adequately warn. Some claim that the onus falls on the doctor to adequately treat his or her patients and, as a result, to choose the medicine that is right for each individual patient. In most cases, however, physicians will prescribe a drug even with the knowledge that it has certain adverse side effects because the information available to them, from medical journals and clinical trials outlined in the drug's prescribing information, describes the risk of any adverse event occurring as miniscule; as a result, the benefit to the patient exceeds the health risk posed by such a drug. Thus, it is difficult to blame physicians for using the information proffered by the respective pharmaceutical company claiming that the drug is safe in making informed decisions regarding the health of their patients.

Conversely, many physician advocacy groups blame the pharmaceutical companies' desire to gain the most market share and revenues.[153] They claim that the pharmaceutical companies continually mislead physicians by feeding them erroneous information through their sales representatives or failing to disclose vital information regarding the drug's safety.[154] For instance, during the Vioxx Senate Hearings,[155] critics claimed that Merck purposely misled physicians by compensating their sales representatives with a bonus program, which provided the representatives with an incentive not to disclose fully Vioxx's safety issues in an effort to increase the drug's market share.[156] This program allegedly directed representatives to find ways to avoid safety related questions from physicians and handle these "obstacles" before reverting to the message promoting the drug's efficacy.[157] In response to such criticism, a Merck

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about the changes at the FDA over the years, but also warned that "approval times have been cut in half, and the percentage of new drugs being introduced in the United States before being introduced in other countries has nearly doubled." *Id.*

[153] *See, e.g., id.* at 82-87 (statement of Abbey S. Meyers, President, The National Organization of Rare Disorders) (discussing problems with the Prescription Drug User Fee Act).

[154] Tansey, *supra* note 151.

[155] *Id.* Representative Henry Waxman (Democrat) of Los Angeles, California, stated at a hearing of the House Government Reform Committee that Vioxx "built up sales topping $2 billion during a period when safety concerns were mounting among scientific experts and federal regulators." *Id.* Representative Waxman, whose staff analyzed 20,000 documents related to the sales promotion of Vioxx, also claimed that physicians wrote millions of Vioxx prescriptions due to "Merck sales strategies that amounted to 'disinformation and censorship'." *Id.*

[156] *Id.*

[157] *Id.* In addition, the committee analysis found that sales representatives were not to initiate discussions of the Vioxx VIGOR study with physicians and "[i]nstead, they were to offer information from a company-prepared 'cardiovascular card' that indicated Vioxx was eight to [eleven] times safer than other anti-inflammatory painkillers." *Id.* The VIGOR study showed that although efficacious, Vioxx did have a higher risk of causing cardiovascular events than naproxen. Press Release, Peter S. Kim, President, Merck Research Laboratories (Oct. 13, 2004), *available at* http://www.merck.com/newsroom/vioxx_withdrawal

spokesman further reiterated that the company's marketing practices were fair and balanced, noting that physicians have the opportunity to read every clinical study including Vioxx.[158] In addition, these sales practices are common throughout the pharmaceutical industry where sales representatives attempt to persuade busy physicians to use their products and as a result often fail to be objective. Nevertheless, the FDA found that Merck's sales practices were legal and appropriate.[159]

D. Shared Culpability Among All Parties Involved?

Inevitably, the party solely responsible for a drug withdrawal is not easily discerned. As evidenced by the Vioxx case and other recent drug withdrawals, it is usually a combination of missteps by both the drug's manufacturer and the FDA. Ultimately, it is difficult to assess blame but easy to identify those who are adversely affected. For instance, it may be the patients who relied on the information provided to them by doctors. Additionally, it may be the doctor who relied on information provided to him or her by the pharmaceutical company. Finally, it may be the pharmaceutical company and the appropriate regulatory agency that were unaware of the dangers of a drug that had not yet been fully investigated.

VIII. POSSIBLE SOLUTIONS

There are several possible solutions in order to minimize the numerous ways in which a drug withdrawal may affect multiple parties. First, although a drug may negatively affect certain patients, other patients who are positively affected by the drug are faced with a lesser quality of life as a result of the drug withdrawal. These patients might be able to find some relief if the withdrawn drug could still be prescribed to them. For instance, in the VIGOR trial, Vioxx was administered to 4,000 patients, some elderly, at the highest possible dose of fifty milligrams.[160] Most patients who were prescribed Vioxx, however, were often younger patients and were prescribed much lower doses, specifically at 12.5 and 25 milligrams.[161] Therefore, many of the patients who were previously prescribed Vioxx did not fall into the category of patients who experienced problems in the VIGOR trial and arguably should be allowed to continue using it at the lower dose.

/pdf/10_13_2004_psk.pdf.

[158] Tansey, *supra* note 151.

[159] *Id.*

[160] Letter from Thomas W. Abrams, Dir. of Div. of Drug Marketing, Adver., & Commc'ns, U.S. Dep't Health & Human Servs., to Raymond V. Gilmartin, President and CEO of Merck & Co. Inc. (Sept. 17, 2001), http://www.fda.gov/foi/warning_letters/g1751d.pdf.

[161] FDA.gov, Vioxx (rofecoxib tablets and oral suspension), http://www.fda.gov/medwatch/SAFETY/2002/vioxx_PI.pdf (last visited Feb. 24, 2007) (prescribing information circular).

In fact, several months after Vioxx was withdrawn from the market, a joint advisory committee of the FDA, including thirty-two experts, concluded that Vioxx should be permitted to reenter the market with a stronger warning.[162] The committee put forth such a recommendation because it concluded that in certain patient populations, the benefits may outweigh the risks.[163]

A. Allow the Withdrawn Drug to Reenter the Market Under Restricted Conditions

There has only been one case in U.S. history where a drug that was previously withdrawn from the market was allowed to reenter. In 2000, Glaxo Pharmaceuticals introduced Lotronex, which treated irritable bowel syndrome and as a result helped millions of Americans inflicted with this painful illness.[164] Just nine months after it had received FDA approval, however, the drug was connected with the deaths of seven individuals, and it was pulled from the market.[165] Nevertheless, after heavy lobbying from desperate patients claiming it to be the only drug that ever relieved their constant misery, the FDA permitted Glaxo to reintroduce the drug into the U.S. market under careful scrutiny and only if the company agreed to increased monitoring.[166] Currently, "Lotronex may be prescribed only by certain doctors enrolled in a special program, and given only to the sickest patients – fewer than 5% of sufferers – who have failed other therapies."[167]

The Lotronex incident proved that a withdrawn drug may be allowed to reenter the market under careful scrutiny because certain patient demographics whose quality of life is negatively affected by the drug's withdrawal may suffer less harm with the drug than without it. Nonetheless, the manner in which the drug will be tested and scrutinized must be carefully evaluated before the drug can be placed back on the market. Also, the FDA must conclusively find that the drug is safe for the patient populations that would be allowed to use the drug. Finally, the FDA must still be willing to re-pull the drug back off the market if there is even a remote chance that the drug will pose any health risk to these patients.

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[162] *Vioxx Could Be Sold Again*, *supra* note 143. A stronger warning may be in the form of a black box warning, which is placed in the drug's prescribing information regarding a possible adverse side effect from use of the drug. Other such warnings also include "Dear Doctor" letters, whereby the FDA informs any prescribing physician of the possible dangers associated with the drug in question.

[163] *Id.*

[164] *Bowel Drug Returns to Market with Restrictions*, USA TODAY, June 7, 2002, http://www.usatoday.com/news/health/2002-06-07-bowel-drug.htm.

[165] *Id.*

[166] *Id.*

[167] *Id.*

B. Create Medical Liability Review Panels in Order to Reduce the Number of Frivolous Lawsuits

Usually, after a drug is withdrawn from the market, plaintiffs' attorneys create a public hysteria of sorts by soliciting past users of the drug. As a result, many frivolous lawsuits are filed, costing the pharmaceutical company millions of dollars in litigation costs and negative publicity. In order to reduce the number of frivolous lawsuits that are filed, many states either require or permit that the claim first be submitted to a medical liability review panel that will determine the credibility of the claim and whether standing may be established in order to further pursue litigation.[168] This approach, requiring submission of cases to review panels consisting of doctors and lawyers, was first enacted by a number of state legislatures in order to "aid the early settlement of cases."[169] As a result, the state legislature will ensure that the court's time is not being wasted and that pharmaceutical companies are not subjected to the added costs of defending against frivolous claims.

C. Create an Independent Drug Monitoring Board

Another possible preventive solution is to institute a drug monitoring board independent of the FDA.[170] This board would only be in charge of monitoring drug safety for high volume drugs on the market. It would monitor the appropriate clinical trials and submit reports to both the FDA and PhRMA in order to ensure compliance with recommendations. Nevertheless, the goal of such a board would be to decrease the FDA's workload and create an independent body, detached from the pharmaceutical industry and the FDA, that would be able to monitor objectively pharmaceutical drugs from beyond the reach of pharmaceutical lobbyists.[171] This board could also ensure that money is being spent on improving existing products. As the President of PhRMA, Alan F. Holmer, stated during his congressional testimony:

> The industry is spending more than $30 billion annually on research and development [referring to the 2002 year], with about eighty percent of this investment dedicated to the advancement of scientific knowledge and the development of products, compared to about twenty percent that is devoted to improving and/or modifying

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[168] Frank P. Grad, *Medical Malpractice and the Crisis of Insurance Availability: The Waning Options*, 36 CASE W. RES. 1058, 1082 (1986).

[169] *Id.*

[170] JERRY AVORN, POWERFUL MEDICINES: THE BENEFITS, RISKS, AND COSTS OF PRESCRIPTION DRUGS 373 (2004).

[171] Matthew Harper, *David Graham on the Vioxx Verdict*, FORBES.COM, Aug. 19, 2005, http://www.vioxx-recall-lawsuit.com/news/graham.pdf.

existing products.[172]

Currently, the FDA is charged with monitoring more than 10,000 drugs, in addition to performing other regulatory duties such as new drug approval and post-approval marketing surveillance.[173] An independent monitoring board would therefore mean that there are some checks and balances in the system and would allow for closer scrutiny of post-approval clinical studies.

Therefore, there are several possible solutions to reduce the devastating impact such withdrawals have on all the affected parties.

IX. CONCLUSION

The pharmaceutical industry has played a prevalent role in both United States and world history. Pharmaceutical companies have been credited with eliminating many diseases through the introduction of novel medicines and, as a result, are helping to increase life expectancy rates throughout the world. In order to continue to develop novel medicines, however, pharmaceutical companies place a great deal of emphasis on research and development. Research and development cost a company millions of dollars every year in its search for the next blockbuster drug. Much expense is placed on obtaining the best and brightest scientists and providing them with the requisite resources to produce a blockbuster drug. In order to provide scientists with the resources required to produce the next blockbuster drug, a pharmaceutical company must gain sufficient revenue from its existing pipeline of drugs. Hence, a cycle in which a company is forced to produce blockbuster drugs in order to offset the costs of previous blockbuster drugs.

Today, pharmaceutical conglomerates are bigger than ever. Presently, more money is spent on obtaining the brightest executives and providing sales personnel with all the resources necessary to obtain the greatest possible market share in this very competitive industry. The company depends on a strong pipeline of drugs that will provide a continual stream of revenues and profits for this purpose as well. This stream of revenues and profits is required in order for the company to produce novel medicines.

As a result of being a player in a very competitive industry, pharmaceutical companies in the United States have the dual objective of providing affordable healthcare to the general public and making a profit for their shareholders. As consumers have demanded more affordable medicines, pharmaceutical companies and the FDA have developed an increasingly cozy relationship and, as a result, have put the public at risk.[174] This is a contentious proposal for

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[172] GOOZNER, *supra* note 12, at 235.

[173] *See* Michelle Meadows, *Why Drugs Get Pulled Off The Market*, FDA CONSUMER, Jan.-Feb. 2002, at 11, 11-17, http://www.fda.gov/fdac/features/2002/102_drug.html.

[174] *See, e.g.*, Eric J. Topol, *Failing the Public Health – Rofecoxib, Merck, and the FDA*,

many pharmaceutical executives, knowing that they are only as secure as the next dividend payment to their shareholders. Therefore, such executives must produce more profitable blockbuster drugs or else find other employment.

The continual desire to produce the next great blockbuster drug can lead to many legal, business, and ethical problems. As a result, when a pharmaceutical company produces a blockbuster drug that is later pulled off the market because of safety concerns, the question arises as to whether the lure of making a profit blinded the company into approving a drug wrought with safety issues. Regardless of the circumstances prompting a company to pull a drug off the market, the ramifications of such a decision can affect all involved, including company employees, physicians, patients, and the appropriate regulatory agencies.

The legal, business, and ethical ramifications of pulling a drug off the market can be severe. This removal can cost the company millions of dollars in litigation as a result of the multitude of lawsuits brought by the alleged victimized plaintiffs claiming that the company produced an unsafe product.[175] The costs of a drug withdrawal can affect the company in more ways than just its bottom line. For instance, it can affect a pharmaceutical company's perception on Wall Street and, as a result, affect investor confidence. Since most large pharmaceutical conglomerates are traded on publicly accessible stock exchanges, a major drug withdrawal can cause a decrease in stock price. Therefore, the loss in investor confidence ultimately leads to a variety of changes within the respective pharmaceutical company. Restructuring leadership positions can include layoffs and termination of many executive positions.

Finally, there are significant ethical questions to be answered after a drug has been withdrawn from the market. Specifically, how are patients to cope when they have depended on the withdrawn drug to provide them with a quality of life that they did not possess prior to the drug's introduction in the marketplace? Moreover, when did the FDA and the respective pharmaceutical company know of the drug's safety issues and was the response swift and appropriate? The ideal solution would be for the pharmaceutical companies to take these questions into account both prior to marketing the blockbuster drug and every step of the way after initially marketing it.

After examining the different parties affected by a drug withdrawal, there is no one party who is clearly culpable. Although at first it seems as if the pharmaceutical company must be blamed,[176] in essence, there are many parties that are blameworthy. To solely blame one party over another, however, would be erroneous because, ultimately, the parties negatively affected by a drug

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351 NEW ENG. J. MED. 1707, 1707-09 (2004); THOMAS L. FRIEDMAN, THE WORLD IS FLAT: A BRIEF HISTORY OF THE TWENTY-FIRST CENTURY 252 (2006).

[175] On the other hand, patients who were negatively affected by the drug must spend considerable time and money to sue a defendant who more often has considerably greater resources.

[176] *See generally* BARRY WERTH, THE BILLION DOLLAR MOLECULE: ONE COMPANY'S QUEST FOR THE PERFECT DRUG (1994) (illustrating the importance that a company places on profits and finding the next blockbuster drug).

withdrawal are also those in fervent support of developing and distributing effective drugs.