consideration to how particular organizational or philosophical beliefs within a corporation or regulatory structure could influence the occurrence of corporate crime.

More recent work has moved from general assumptions to an examination of particular organizational impacts on corporate crime; not surprisingly, through detailed case studies. Diane Vaughan's *Controlling Unlawful Organizational Behavior: Social Structure and Corporate Misconduct* she describes how an antiquated regulatory reporting system was at least partially responsible for the perpetration of corporate crime by two corporate officers from the Revco Drug Store Chain in Ohio. Likewise, Gary Schwartz's The Myth of the Ford Pinto Case" and Matthew Lee and M. David Ermann's "Pinto 'Madness' as a Flawed Landmark Narrative: An Organizational and Network Analysis" each described how a lack of communication between work groups at the Ford Motor Company, an adherence to conventional goals within the automobile industry and evolving safety regulations caused the development of what many believed was a flawed and dangerous automobile responsible for considerable social harm (the Ford Pinto). Their analyses have challenged more critical accounts of Ford's conduct in the Pinto case – ones which conclude that the company's behavior was definitively criminal – by placing Ford's particular organizational decision-making within a wider corporate and regulatory context.

Vaughan' account of the Revco case begins in May of 1976, when a pharmacist working at a Revco Drug Store, located in the state of Ohio, noticed a podiatrist was prescribing large amounts of narcotics and tranquilizers. The pharmacist, believing this pattern of prescribing medicine was suspicious, called the Ohio State Board of Pharmacy to report the podiatrist. Two months later, a vice president of Revco

encouraged the Board of Pharmacy to pursue an inquiry into the prescribing patterns of the podiatrist, even allowing the board access to Revco billing records. Ironically, this particular instance of good conduct by a corporate officer would subsequently lead to the exposure of large-scale bad conduct by the same corporation. An investigation revealed that Revco had received $521,521.12 from the Ohio Department of Public Welfare by double-billing 63,847 prescriptions to the state Medicaid program (Vaughan, 1983).

Although a coordinated undercover investigation had been conducted by several Ohio state law enforcement agencies, the clandestine aspect of the operation turned out to be unnecessary. After search warrants were served on five Revco drug stores, a letter was sent from a prosecutor's office to the corporation and the corporation was given notice that all reimbursements from Medicaid would be suspended; the corporation volunteered to cooperate and aid in the investigation. It was soon discovered that a vice president of Revco and a program manager were responsible for the fraud.[10] The two company employees had not committed the scheme as any sort of embezzlement or what they believed was unjust enrichment of the corporation. Instead, what investigators and state officials considered fraud, had merely been a way to recoup reimbursements for over fifty thousand claims rejected by Medicaid. The claims had not been rejected by Medicaid because they were unwarranted; the claims were rejected due to errors found by a state Medicaid computer program. A new computer system implemented by the Medicaid resulted in system breakdowns, claim backlogs

[10] Vaughan recounts the vice president was a former pharmacists and the program manager had extensive knowledge of computing software. Thus, both had specialized knowledge how to develop a plan that would be unlikely to alert the Ohio State Department of Public Health.

and infrequent reimbursements for claims. To alleviate these problems, it was expected that pharmacies seeking Medicaid reimbursement install presubmission edit software to reduce the number of rejected claims. Revco installed the recommended software, but it did not work properly. This problem was compounded by the welfare system constantly updating its own system and making changes to the information required by providers. After Revco agreed to a guilty plea[11] and to pay restitution, both Revco and the welfare office made changes which resulted in less rejected claims. As Vaughan notes, Revco committed criminal actions to recoup payments they were owed due to the inefficiencies of a state bureaucratic agency. Yet, given the resources and complexity involved in perpetuating a double-billing scheme to recoup the payments; perhaps Revco could have used the time and effort to correct the rejected claims or fix their computing problems instead (Vaughan, 1983).

Problems with the Ford Pinto were first documented by Mark Dowie (1977). In his article "Pinto Madness," he described a callous company president (Lee Iacocca) rushing a car into production with profit concerns trumping the safety of American consumers with tragic results. Hundreds of Pinto owners were burned to death in rear-end collisions. Dowie argued these collisions could have been prevented if the automobile was not rushed into production and if the automobile maker had been willing to spend twenty to thirty dollars more per car. In what is now widely employed as one of the preeminent examples of corporate greed, the Ford Motor Company stuck rigidly to a cost-benefit analysis. According to the analysis, paying off successful lawsuits was

[11] Revco had its record of the guilty plea expunged five years later as a result of the conviction being a first offense, no further criminal actions occurred and Revco had rehabilitated the image of the corporation (Vaughan, 1983).

cheaper than a recall of the existing automobiles. Additionally, the Ford Motor Company (as well as other automobile manufacturers) consistently resisted the implementation of tougher standards for automobile safety. Lee Iacocca had wanted to produce an automobile that cost under $2,000 and was willing to cut corners to accomplish this goal. Cullen, Maakestad and Cavender (1984) document the well-publicized, but unsuccessful prosecution of the Ford Motor Company in an Indiana state court for reckless homicide based upon their conduct in manufacturing the Ford Pinto.[12] Eventually the Ford Motor Company conducted a recall of the Pinto citing public relations concerns rather than admitting to defects in the automobile (Schwartz, 1991).

After the initial furor surrounding the Ford Pinto, a few scholars reevaluated the case of the Ford Pinto and reached dissimilar conclusions to the first generation of studies which had so fervently criticized the Ford Motor Company. Schwartz (1991) notes that although Ford knew there were problems with the crashworthiness of the Pinto, standards set by the National Highway Transportation Safety Bureau (NHTSB) mandated that automobile manufacturers comply with newer and more stringent safety guidelines by 1977, which the Ford Motor Company complied with in newer models of the Ford Pinto. The cost-benefit analysis, which Dowie had mentioned in "Pinto Madness," actually referred to the potential damages from rollovers of the automobiles, not rear-end collisions. In one lawsuit, the plaintiffs tried to proffer the report as

[12] The Indiana reckless homicide statute became effective on October 11, 1977. The constitutional prohibition against ex post facto laws prohibited any conduct by the Ford Motor Company before that date to be introduced at trial (Cullen et al., 1984; Schwartz, 1991).

evidence of corporate mentality when calculating punitive damages, however, the presiding judge ruled the report inadmissible.[13]

Lee and Erdmann (1999) argued there was a lack of communication or coordination between different divisions within the Ford Motor Company and that no one person knew of all the potential problems associated with the Pinto. If there had been better coordination between divisions responsible for developing different parts and systems within the automobile, safety problems may have been easier to diagnose and changes to the Pinto might have been implemented earlier. Lee and Erdmann argued that not only did employees of the Ford Motor Company believe the cars the company designed and manufactured were safe; many employees drove them, as well as their family members. Additionally, considering that safety standards within the industry were new and developing, engineers at Ford believed that subcompact automobiles (the class of automobile to which the Pinto belonged) by their very nature are less safe than larger automobiles. Automobiles in the same class produced by rival manufacturers were more dangerous than the Pinto. Lastly, these rival subcompact automobiles were designed and built according to the same budget restrictions to that of the Pinto, yet Ford had been singled out for vilification.

Dowie's account of the problems associated with the development of the Ford Pinto makes for compelling reading and his narrative is the embodiment of every negative belief or stereotype of corporate behavior. The flaws in Dowie's analysis, however, are well illustrated by the work of Schwartz as well as Lee and Erdmann. Furthermore, Dowie failed to contextualize the behavior of the Ford Motor Company

[13] A $200,000 valuation of the price of a human life that had been attributed to the Ford Motor Company was actually developed by the NHTSA (Schwartz, 1991).

within the automobile industry as whole. All automobile manufacturers manufactured subcompact automobiles to similar standards and presumed that most people would naturally understand that these automobiles were less safe than larger models. The Ford Pinto was actually safer than several competing models produced by rival automobile manufacturers. Additionally, Dowie assumed that all actors within the corporation were working together in concert. Instead, the corporation that invented the assembly line and division of labor did not properly develop lines of communication between divisions and employees. Lee Iacocca did not design or build Ford Pintos himself, he relied on different engineers to design and build an automobile to the specifications that Iacocca desired.

Considering the complexity of unraveling and identifying harms perpetrated by corporations, a framework is needed to evaluate to properly analyze if the actions or inactions of corporations should be considered criminal. Laufer (1994) argues that four different models are present in the literature to guide the determination of whether a corporation will be liable for the actions of their employees: proactive fault, reactive fault, corporate ethos, and corporate policy. Proactive fault seeks to ascertain whether the practices or procedures of a corporation are inadequate to prevent crimes by their employees. To avoid criminal liability, corporate officials should establish oversight procedures and exercise due diligence to prevent criminal actions by their employees. Reactive fault, as proposed by Braithwaite and Fisse (1990), seeks to analyze what actions corporate actors took after discovering the criminal activities of their employees. Therefore, an actus reus of a criminal employee will not be imputed to the corporation until they fail to report these actions or take actions against the employee. Corporate

ethos seeks to analyze the organizational behavior or culture of a corporation. To impute the criminality of employees to a corporation, based upon corporate ethos theory, one should seek to understand if the policy goals of the corporation either encourages or promotes criminal actions by its employees.

Similar to corporate ethos is corporate policy (Laufer, 1994). This concept states that "corporate actions are not simply the products of individual choice, but the melding of individual decisions set within an organizational structure and embedded in an organizational culture" (Laufer, 1994, p. 668). Such a framework seeks to analyze the corporate structure, including the hierarchy found within. If a criminal act is seen as consistent with the implementation of corporate policy, it may be imputed to the corporation. Furthermore, it is noted that three criteria can directly illustrate corporate intentionality: "a corporate practice or policy violates the law; it was reasonably foreseeable that a corporate practice or policy would result in a corporate agent's violation of the law, or a corporation adopts or ratifies a corporate agent's violation of the law" (Laufer, 1994, p. 668).

State-Corporate Crime

The traditional corporate crime paradigm, in all of its different manifestations, tended to share a fairly uncritical assumption that the interests of the corporation and the state were antagonistic. That is to say the state either ideally or in reality, was understood to be seeking the regulation of corporate behavior to protect the public interests, while corporations sought to avoid that control to pursue its own interests. The emergence of critical criminology (and Marxist criminology more generally) brought with it a questioning of the state-corporate relationship. Numerous influential historical-

sociological studies in the 1960s introduced a corporatist narrative of the state, in which the state sought to protect corporate interests. Critical criminologists argued that in a capitalist society the legal system should be seen as primarily a tool of corporations (Chambliss, 1989; Quinney, 1974, 1977).

According to Michalowski and Kramer (2006) "Great power and great crimes are inseparable…When economic and political powers pursue common interests, the potential for harm is further magnified" (p. 1). They argue that when these two forces come together, state-corporate crimes occurs: "state-corporate crimes are illegal or socially injurious actions that occur when one or more institutions of political governance pursue a goal in direct cooperation with one or more institutions of economic production and distribution" (Kramer and Michalowski, 1990, p. 4). The indictment of state action and political decision-making in their work is extensive and strongly worded: "Modern history is dense with crimes flowing from decisions taken by economic and political elites…from the physical and cultural destruction of Native people…to the world wars, aerial bombings, genocides, and ethnic displacements…political leaders have authorized the ruination of unaccountable millions of innocent human lives" (Michalowski & Kramer, 2006, p. 1).

Within the state-corporate crime literature, two types of state-corporate crime have emerged: state initiated and state facilitated (Kramer, Michalowski & Kauzlarich, 2002). "State-initiated corporate crime…occurs when corporations, employed by the government, engage in organizational deviance at the direction of, or with the tacit approval of, the government" (Kramer et al, 2002, p. 271). One example of state-initiated crime was the explosion of the Challenger space shuttle which resulted in the

death of six astronauts and Christa McAuliffe, a school teacher. Kramer (2006) argues that the Challenger explosion was not an accident and was the result of a flawed design largely promulgated by budgetary restrictions, the National Aeronautics & Space Administration (NASA) being allowed to essentially regulate itself and the interaction between a government agency (NASA) and a private corporation (Morton Thiokol, Inc.).[14]

The second type of state-corporate crime is known as state-facilitated corporate crime. Kramer et al (2002) argue this type of crime occurs when regulatory agencies or institutions fail to restrain deviant business activities perpetrated by corporations. This can occur either through direct collusion between corporations and government or as the result of the shared goals of these two parties which the attainment of would not be possible or made more difficult by aggressive government regulation. An example cited as state-facilitated corporate crime was a fire at an Imperial Food Products chicken-processing plant in Hamlet, North Carolina that killed twenty-five plant employees and injured an additional fifty-six. Aulette and Michalowski (1993)[15] argue that the state of North Carolina "facilitated" this crime because the state was friendly to business interests in the state and provided very little oversight, to the detriment of employees at these facilities. Additionally, Aulette and Michalowski argue that the state of North Carolina lacked a commitment to the state's Occupational Safety and Health Program; even returning $453,000 in earmarked monies to the federal government. Such

[14] For a different and more comprehensive account of the Challenger explosion see Vaughan (1990; 1996). She does not use the word "crime" in her analysis of the events leading up to the Challenger disaster. See also Perrow (1999). He argues that as we embrace technologies that are more complex, accidents will occur, a phrase he refers to as "normal accidents."

[15] A Google scholar search shows this study has been cited thirty times in the literature.

conditions led plant managers to provide inadequate escape routes from the plant, which resulted in an organizational culture in which the owners of the plant were allowed to lock the doors of a facility during hours of operation, which contributed directly to death and injury. The plant managers would not have made these callous decisions if they did not know there was only a miniscule chance of an inspection by state authorities.

The state-corporate crime paradigm has been further developed in several detailed case studies of social harm deriving from corporate behavior and state regulatory decisions. Matthews and Kauzlarich (2000) argue that ValueJet and SabreTech (an airline maintenance company) did not comply with safety regulations regarding the storage of hazardous materials on airline flights. This, combined with the inadequate enforcement of such regulations by the Federal Aviation Administration (FAA), constituted a state corporate crime and led to the crash of ValueJet Flight 592 on May 11, 1996 in the Florida Everglades. 105 passengers and five crew members were killed in the crash. Kauzlarich and Kramer (1998) argue that the production of nuclear weapons has led to the criminal contamination of the environment. Mullins (2006) argues that the high number of tire tread separations of Bridgestone-Firestone tires, which caused many rollovers of Ford Explorers and the failure of the government to address the problem until three years after notice of the problem represented a state-corporate crime. Cruciotti and Matthews (2006) argue that the Exxon Valdez oil spill was a result of the decisions made by Exxon, Alyeska Pipeline Service Company, the U.S. Coast Guard, the state of Alaska, and the United States government generally.

The state-corporate crime paradigm is at its best when it can be used to examine how organizational dimensions of both corporations and the state can lead to socially injurious acts and in particular the interactions of these organizations with one another. The use of the term state-corporate crime has placed many criminologists on the defensive in attempts to justify the use of the word "crime" while referring to the state (Kramer, 1985; Michalowski and Kramer, 1987; Muncie, 1996). Faust and Kauzlarich (2008) argue that the reactions (or perhaps inaction) of federal and state government agencies during Hurricane Katrina represented a state crime of omission. Kramer et al. (2002) tries to bypass this problem by using the terminology *state-corporate crime victimization*, and Harper and Israel (1999) try to further separate themselves from the crime dilemma by using the terminology *state-corporate victimization*. According to Harper and Israel (1999) "…definitions of crime as dynamic rather than static, reflecting not only changes in the law but changes in attitudes towards various forms of acts and omissions. In this sense, societies create crime because they construct the rules whose transgression constitutes crime" (pg. 2). From this viewpoint scholars can focus on quantifying what are socially injurious behaviors outside of legal constructions.

States, Corporations, and Crime: Social and Institutional Environments

One of the great limitations of the state-corporate crime model is that it assumes a relatively direct, binary relationship between essentially singular actors. This assumption can result in analysis that treats that binary relationship as the sole object of study, without considering the social and institutional environments in which that relationship exists. It also runs the risk of re-simplifying the corporate actor and treating the state as a one dimensional object – both making an individual amoral calculation. In

her analysis of the Revco case, Vaughan (1983) concluded that in some cases strict regulations, complex rules and uncaring bureaucracies can actually encourage the commission of crime. Although their actions were wrong, the two corporate actors at Revco only committed a crime to secure money the corporation was owed. The scheme ended when the company had secured reimbursement. Furthermore, the two corporate actors were never encouraged to commit crime to secure the reimbursements. Indeed, it was good faith on the part Revco which allowed the reimbursement scheme to be discovered in the first place.

Lee and Ermann (1999) argued that corporate and state decision making needed to be placed within a larger interorganizational network. The decisions of the Ford Motor Company cannot be properly evaluated unless they are considered within the proper context. The automobile industry, the court system, the NHTSA and other government agencies all affect how automobiles are developed and manufactured. This meant that the outcomes in the Pinto case had to be understood as the product of the assumptions and forces at work in a complex network that included multiple companies, multiple state actors and private interest groups. Both Vaughan and Lee and Erdman seem to argue that a better understanding of the decision making environment within corporations is needed.

One common theme relevant to the pharmaceutical industry and the regulation structure is how risk assessments are conducted. When assessing the decision-making that led to the explosion of the Space Shuttle Challenger, Vaughan (1990, 1993) argued that NASA was essentially allowed to self-regulate and received little to no oversight. This situation allowed for a culture to grow within the agency that would not only

minimize the assessment of risk, but actually discourage the reporting of problems that could result in delaying space shuttle launches. Such a culture, which discourages the reporting of risk, leads to deviance and eventually problems within the agency. In the case of NASA, it led to the loss of a space shuttle and the deaths of all on board. Many observers have noted similar problems within the pharmaceutical industry when it comes to cultures of risk assessment (Braithwaite, 1984; Clinard & Yeager, 1980; Comanor, 1986; Simon & Sitzen, 1990).

Cultures of risk assessment are not simply the product of individual corporate or regulatory organizational structures. Rather, they exist with a broader social context. One way of illustrating this is the assessment (and balancing) of short-term versus long-term risk. Maines (2005) notes that asbestos was used during much of the industrial era to prevent fire and protect against heat, acids and electricity. At one time, asbestos was found in nearly three thousand products and was credited for saving countless lives and protecting many cities and industrial areas from the grave risk of fire. However, this protection came with a long term cost. Long-term exposure to asbestos produced many chronic health problems and the reputation of the material is quite different today than it was at mid-twentieth century. Yet, the question still needs to be considered – how many people would have died had asbestos not been used so often? Some of the people that suffered from long-term exposure to asbestos may not have lived long enough to suffer long-health problems had it not been for the short-term protection the material offered. More importantly, the answer to these sorts of risk assessment and risk balancing questions are not likely to be produced by or confined to particular organizations, but reflect the input of many social groups.

The risk assessment/risk balancing is particularly important to the history of decision making within the pharmaceutical industry. Drugs can make people's quality of life better or worse. In some instances drugs save lives, in others they might take lives. Doctors, medical researchers, patient advocacy groups and the ill and their families can all exert pressure to open up increased access to drugs, thus placing greater weight on the short-term rather than long-term calculation (and certainly greater weight on the potential therapeutic benefits of a new drug, versus the potential harms – short term or long term). At various times, each of these interest groups have claimed that the FDA is far too cautious with the drug approval process and should actually streamline or eliminate various steps in the approval process. In a few cases, a desire for non-approved drugs (within the United States) has led to these drugs being smuggled from foreign countries that have already given them approval or do not restrict access to them. Therefore, to properly consider whether the actions of Purdue Pharma and state actors that were entrusted with a duty to protect the American people from the harms associated with OxyContin® constituted a state-corporate crime, a study of the historical development of the pharmaceutical industry and the state apparatus for the regulation of the industry will be considered in the next chapter.

CHAPTER 3
THE PHARMACEUTICAL INDUSTRY AND STATE REGULATORY RESPONSE

Edwin Sutherland's 1939 Presidential Address included the pharmaceutical industry as one of the most consistent corporate criminal offenders, whose conduct frequently worked against the public interest. He observed that 140 pure food and drug bills had been introduced in Congress between 1876 and 1906 before one of real substance (The Pure Food and Drug Act) had been passed. Sutherland was hardly the first to accuse the drug industry as one especially prone to causing social harm, as all of the defeated nineteenth century drug bills suggest (Sutherland, 1983).

Perhaps the greatest concern regarding the pharmaceutical industry is the safety of drugs once they are marketed and distributed (Backhaus, 1983; Braithwaite, 1993; Lasagna, 1969; Olson, 2002). There is a substantial range of social harms associated with drug products in the legal marketplace. Many drugs have serious side effects, individually, or in combination with other drugs. These side effects can range from minor inconveniences to lasting harms and in some cases even fatal drug reactions. An overreliance on the prescription of drugs therapeutically can also lead to physicians failing to properly evaluate and diagnose a patient or lead to a false hope that all medical problems can be solved by drugs (Lasagna, 1969). Drugs are subject to abuse, or may create a dependency in their users. And, of course, drugs in the legal marketplace may be diverted into underground or illegal markets, where they may be further misused.

On the other side of the ledger, regulatory policy had always had to take into account concerns of maintaining appropriate levels of practitioner and consumer access to new medications. Olson (2002) notes, for example, that various interest groups have

repeatedly complained that the FDA takes too much time to evaluate drugs during the approval process. As a result, the FDA has streamlined certain stages of the approval process resulting in quicker decisions. This chapter reviews more than a century of state regulatory response to the drug industry. The chapter concludes with a more thorough review of the rise and development of the particular state-pharmaceutical industry regulatory system – the abuse liability assessment system – whose failure is at issue in the case of OxyContin®.

State Regulatory Response

The Pure Food and Drug of 1906 was not the first piece of federal drug regulation passed due to a public health scare, nor would it be the last. During the Mexican-American War (1846-1848) more American soldiers died from disease than from the battlefield. Although at the time few medicines could have cured many of the ailments that afflicted the soldiers[16], the adulterated, impure and diluted medicines that had been provided to soldiers were widely condemned and led to the passage of the Drug Importation Act of 1848. This law required that all drugs imported into the United States be inspected for both purity and quality. The law was ineffective in that it did not set any standards for either purity or quality and delegated enforcement of the law to customs officials without providing them any training to carry out the new duty (Hawthorne, 2005).

Although many conceive of pharmaceutical companies as selling their wares via pharmacies to patients who have a prescription from a licensed physician, this has not always been the case. In the late nineteenth century, pharmaceutical companies

[16] Such as cholera, dysentery and yellow fever (Hawthorne, 2005).

routinely marketed and sold drugs to the general public for self-medication purposes. Commonly known as “patent” medicines, these drugs promised to virtually cure all ailments one might suffer from. No governmental regulations existed that curtailed advertising claims and these “medicines” were not required to list the ingredients in their formulas (Courtwright, 1982, 2001; Gahlinger, 2004; Goode, 1999; Hawthorne, 2005; Musto, 1999; Spillane, 2000). One of the primary reasons that these drugs were called “patent” medicines was so that the manufacturer could keep their formulas a secret (Fischelis, 1938). Not only were the formulas a secret, patent medicine firms launched one of the first competitive marketing campaigns in American history dating back to just after the American Revolution (Young, 1960). As a result, patent medicines could be purchased nearly anywhere (Courtwright, 1982, 2001; Gahlinger, 2004; Goode, 1999; Hawthorne, 2005; Musto, 1999; Spillane, 2000). Taken in historical context, the near ubiquitous advertising of contemporary pharmaceutical companies might not seem so out of place.

There is no question that the advertising and promotions by patent medicine distributors frequently concealed the presence of dangerous and habit-forming substances, including alcohol, opiates, cocaine and cannabis. Some of these deceptive advertising practices ended with the passage of the 1906 Pure Food and Drugs Act, which required that drug manufacturers provide accurate labeling (Friedman, 1994; Gahlinger, 2004; Hawthorne, 2005). Sutherland (1940) observed that 140 pure food and drug bills had been introduced in Congress in the thirty years before the successfully 1906 legislation, whose success he credited to “a highly dramatic performance by Dr.

Wiley" (Sutherland, 1940, p. 8).[17] Still, those 140 failed bills suggest the strength of the opposition, and it may not be surprising to observe that subsequent amendments which would have prohibited making fraudulent statements, concerning drugs, in the press were defeated by intense lobbying efforts of the pharmaceutical industry (Sutherland, 1940). Despite the passage of the Pure Food and Drugs Act, lobbying by the pharmaceutical industry did not end. Sutherland argued (1983) despite the existence of the new law, the pharmaceutical industry continued their lobbying efforts, which resulted in decreased enforcement of the Pure Food and Drugs Act. The Federal Trade Commission made 1,000 adverse decisions to the pharmaceutical industry for their advertising practices. According to Sutherland, the number of decisions should have been much greater considering the ubiquity of false advertising perpetuated by the pharmaceutical industry.

In addition to requiring the labeling of foods and drugs, the first Pure Food and Drug Act gave the Bureau of Chemistry, a department in the Secretariat of Agriculture, the task of enforcing labeling requirements of drugs. The bureau was underfunded and in order to enforce labeling provisions, the bureau had to sue violators in court rather than prosecute them. In 1930, the Bureau of Chemistry and the duty of enforcing the Pure Food and Drug Act were vested in a new bureaucratic agency called the Food and Drug Administration (FDA) (Hawthorne, 2005; Wax, 1995).

If many pharmacists and physicians had their way, around the turn of the twentieth century, there might not have been a need for many of the pharmaceutical

[17] Dr. Harvey Washington Wiley developed the Bureau of Chemistry within the United States Agricultural Department. He was a frequent critic of the pharmaceutical industry and many argued that his criticisms "…often appeared to go beyond all reasonable limits" (Musto, 1999, p. 12).

regulations that exist today. Intellectual property rights, especially concerning patents and trademarks, were not utilized in the pharmaceutical industry at that time; indeed, the pharmaceutical industry was still in its infancy. Many pharmacists and physicians believed that the best way to ensure that medications were either effective or safe were to make the formulas widely available so that other practitioners could use them and medicine as a science would be enriched from the expansion in knowledge. Pharmacists, physicians and especially pharmaceutical companies that seemed to primarily concern themselves with profits were viewed as stifling scientific progress to satisfy their own greed by establishing monopolies within the pharmaceutical industry. Critics of this viewpoint noted that pharmaceutical companies were beginning to invest escalating funds to the development of new pharmaceutical products. If these companies were not in some way rewarded for new discoveries, especially through a short period of exclusive sales that patents granted, pharmaceutical companies would not be able to recoup their investments (Gabriel, 2009).

By the 1930s, a new generation of reformers pressed the argument that the Pure Food and Drug Act of 1906 was ineffective and in need of updating. As before, their efforts to secure a more extensive federal regulatory apparatus bogged down in Congress. It took a dramatic drug-related tragedy to provide the necessary impetus for new legislation expanding the regulatory system. Sulfanilamide, first synthesized in 1908, had proven successful in combating bacterial infections (Ballentine, 1981; Hawthorne, 2005; Wax, 1995). Sulfanilamide was ingested in either capsule or tablet form, but demand existed for Sulfanilamide in a liquid form (Ballentine, 1981; Wax,

1995). To manufacture a liquid form of the drug, diethylene glycol was added[18], a chemical proven to be an excellent solvent, glycerine substitute and moistening agent. It was also used in the production of resins and explosives (Wax, 1995) and as an antifreeze (Ballentine, 1981). Diethylene glycol, however, was not permitted in food production because it had not been proven safe (Wax, 1995). S.E. Massengill, the manufacturer of the drug, called their new drug Elixir Sulfanilamide (Ballentine, 1981; Hawthorne, 2005; Wax, 1995). 353 patients received Elixir Sulfanilamide during the four weeks it was available in 1937. 105 of those patients died, thirty-four of the dead were children. Many of those who were not killed from the drug only survived because severe gastrointestinal disturbances caused them to discontinue use. Some of the survivors later reported renal failure (Wax, 1995).

In the wake of another public health scare the Food, Drug and Cosmetic Act of 1938 was passed (Ballentine, 1981; Cavers, 1939; Hawthorne, 2005; Wax, 1995). After the passage of the Act, all pharmaceutical companies had to submit a new drug application (NDA) that showed the drug was safe for use before it could be distributed via interstate commerce. The Act also banned drugs that were unsafe for use and prohibited the practice of providing false or misleading labels on drugs. Pharmaceutical companies were required to disclose all active ingredients within a product and provide consumers with recommended uses and warnings about misuse, unless the drug was only available for use by prescription. The Act also gave the newly created FDA enforcements powers that were available in criminal rather than civil courts (Cavers, 1939). The last major impact the Food, Drug and Cosmetic Act had was ushering in the

[18] Also included was raspberry extract to improve the flavor (Ballentine, 1981; Wax, 1995; Hawthorne, 2005).

trend that many medications would only be available being prescription. The 1951 Humphrey-Durham Drug Prescription Act would eventually convert these trends into law (Wax, 1995).

Although the Food, Drug and Cosmetic Act of 1938 was a dramatic improvement over the Pure Food and Drug Act of 1906, deficiencies in regulation still remained. Drug safety was required, but no standards were implemented guiding how animal or human trials were to be conducted. Furthermore, pharmaceutical companies did not have to prove that a drug was effective for the treatment of ailments that they advertised. Unlike the present regulatory structure, the FDA had no involvement or oversight of NDAs until they were filed with the agency. Drugs that had been studied in premarketing clinical trials received exemptions from the review process and if the FDA did not consider a NDA within sixty days, the drug was given approval without review. These deficiencies in the Food, Drug and Cosmetic Act of 1938 would not be addressed by Congress for twenty-three years. (Wax, 1995).

Regulation of the drug industry remerged as a central political issue with the Kefauver drug industry hearings that took place between December of 1959 and October of 1960. Senator Estes Kefauver, at that time, was among the best-known Democratic officeholders in the United States. Kefauver had long used his Senate position to conduct high profile hearings and investigations as a way of boosting his national profile and had held famous hearings on organized crime, juvenile delinquency and the auto and steel industries. A staffer on his subcommittee on antitrust and monopoly complained to the Senator about the high price of prescription drugs and thereby launched a new chapter in Kefauver's political career (Hawthorne, 2005).

The Kefauver hearings began with a focus on prices, questioning drug executives on why there was such a high markup between the cost of manufacturing a drug and the price that pharmaceutical companies sold them to the American consumer. The hearings expanded, however, to an investigation of pharmaceutical advertising practices and, if in addition to proving that new drugs were non-toxic, whether pharmaceutical companies should be required to prove that the drugs they manufacture actually work.[19] Similar to previous legislation, that sought to create more stringent regulation of the pharmaceutical industry, pharmaceutical companies protested additional oversight of their industry. Senator Kefauver found himself without the required support from either the executive or legislative branches of government. However, two years after Senator Kefauver's hearings ended, a new public health scare would provide him with the support to enact his ambitious new regulations with the Kefauver-Harris Amendments to the Food Drug and Cosmetic Act in 1962 (Hawthorne, 2005).

Richardson-Merrill[20] applied for FDA approval of thalidomide on September 12, 1960. Had the drug been given approval, it would have been marketed under the trade

[19] Requiring pharmaceutical companies to prove the efficacy of drugs was important for two important reasons. Although the Food, Drug and Cosmetic Act of 1938 prohibited false or misleading labeling of drugs, without having to prove the efficacy of drugs, this provision was hard to enforce; especially considering pharmaceutical companies were responsible for their own testing. Additionally, a patient taking an ineffective medication will prevent them from taking a medication that is effective.

[20] Thalidomide was not the first dangerous drug that Richardson-Merrill marketed. Mer 29 was introduced to the American drug market in June of 1960 under the trade name Triparanol. At that time, it was believed that high blood cholesterol levels were a leading cause of heart disease, one of the leading causes of death in the United States. Triparanol, according to Richardson-Merrill, was supposed to lower cholesterol levels and immediately became a top-selling drug for the firm. Not only did Richardson-Merrill largely fail to prove that the drug worked as claimed, the firm could not prove that the drug was safe for use either. Side effects from the drug included hair loss, cataracts, and severe forms of dermatitis. In March 1964 Richardson-Merrill, a pharmacologist, a laboratory chief, and a vice president (all employed by the company) pled no contest to two counts of charges of providing false, fictitious and fraudulent statements to the FDA. The company was fined $80,000 and the three employees were given six months

name Kevadon®. Dr. Frances Kelsey was given the application for the drug as her first assignment at the FDA. Richardson-Merrill expected that the drug would be given quick approval and promised that studies would be produced that showed the safety of the drug; something they did not yet have. In a six-point reply to Richardson-Merrill, regarding the approval of thalidomide, Dr. Kelsey pointed out the inadequacy of the studies of the drug and a failure to illustrate the safety of the drug. Rather than conduct further studies, Richardson-Merrill resorted to placing political pressure and misleading Dr. Kelsey's superiors at the FDA about the substance of her report. Dr. Kelsey later read a report in *British Medical Journal* linking thalidomide to peripheral neuritis, a report she believed Richardson-Merrill should have been aware of and should have provided in the drug application. Believing she was being misled, Dr. Kelsey demanded further details about company tests and what evidence there was that refuted reports of peripheral neuritis. On a fact-finding trip to Europe, Richardson-Merrill received bad news. Over four hundred reports of peripheral neuritis had occurred in Germany. Many of these cases showed the condition was irreversible. Despite this evidence, Richardson-Merrill reported back to Dr. Kelsey that reports of peripheral neuritis were overblown, a claim she treated with skepticism. As she noted, a drug company marketing a drug that was not being marketed for life-saving purposes should not be so flippant about reporting side-effects (Knightley et al., 1979).

Richardson-Merrill sent literature reviews to Dr. Kelsey showing that peripheral neuritis was common in other drugs and usually was not permanent. Dr. Kelsey did not respond to the pressure and sent a letter back to Richardson-Merrill stating that the

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probation each. Nearly 500 civil lawsuits resulted in approximately $200 million in damages awarded to plaintiffs (Knightley, Evans, Potter & Wallace, 1979; Rheingold, 1968).

company had not been forthcoming with her. The company was displeased with the letter and considered it potentially libelous. A company vice-president had prepared to take the application directly to the head of the FDA. Before such an action could be taken, however, Dr. Kelsey requested information showing that thalidomide was safe for use during pregnancy. Richardson-Merrill attempted a last ditch effort for approval by requesting when a decision would be made by the FDA on the approval of thalidomide. Realizing that more tests would be required that they could not produce, Richardson-Merrill withdrew the application for thalidomide in 1962 (Knightley et al., 1979).

Shortly after Richardson-Merrill withdrew its application, reports of the link between use of thalidomide in pregnant women and birth defects (most notoriously phocomelia) were widely reported. Although only a few children were born in the United States with birth defects due to thalidomide use, in other countries over eight thousand children were born suffering from birth defects. Countless miscarriages could possibly be attributed to thalidomide had the connection been made earlier. Although Richardson-Merrill did not face any criminal liability from thalidomide, they were not so fortunate in civil court. Most trials went poorly for Richardson-Merrill and were settled out of court before arriving at jury verdicts. Although exact figures are not known, the drug likely cost Richardson-Merrill several million dollars. Had thalidomide actually reached the American market, it has been speculated that damages would have probably cost the company $3 billion. For her role in keeping thalidomide off the American market, Dr. Kelsey was awarded the President's Award for Distinguished Federal Civilian Service by John F. Kennedy. Although her methods and actions have

been the subject of much debate, it has been argued that she received the award for merely doing the job she was assigned (Knightley et al., 1979).

Under the current regulation scheme, the FDA does not actually test the safety of pharmaceuticals (or any other products it regulates) itself, but instead relies on the developing companies to test both the safety, pharmacological effect and health benefits of the drug. To begin this process, a pharmaceutical company must test their proposed drug on animals. After a company completes animal tests, also known as preclinical trials, the company will submit an investigational new drug application (IND) to the FDA. To be successful, this application must clearly describe the results of animal testing, describe the manufacturing process of the drug and provide clear details and guidelines outlining how the pharmaceutical company plans to conduct tests of the drug on human subjects. If the IND is approved, Phase I trials will be conducted. These trials investigate the affect of the drug on a small group of healthy volunteers for the limited purpose of determining if it is safe for human use. If the drug is deemed safe, then Phase II and Phase III clinical trials will be conducted to not only test drug safety, but if the drug is effective (Hawthorne, 2005).

To gain FDA approval for a new drug, a pharmaceutical company must submit a new drug application (including the corporate studies) to the agency, which will be reviewed by physicians, statisticians, chemists, pharmacologists and other scientific reviewers of the Center for Drug Evaluation and Research. Those reviewing the proposed new drug evaluate the company data (describing animal and human testing of the drug) and proposed labeling for the drug. If the health benefits outweigh the known risks of the drug, it will be approved. If previously unknown dangers change this

balance, approval can be later withdrawn or labeling of the drug may have to be altered (Hawthorne, 2005).

Abuse Liability Assessment

Pharmaceutical regulations are not limited to assessments of drug toxicity and efficacy; consideration must also be given to the possibility of patients becoming addicted to the drug and the likelihood that a drug might be diverted to the black market for recreational drug-users. Such analysis is known as abuse liability assessment, which ideally will curb drug misuse and diversion, but not interfere with patient access to medications (Schuster & Henningfield, 2003). Balster and Bigelow (2003) note that it is vital for drug regulation to identify drugs of abuse for the system to properly work. This is not limited to existing drugs; drug regulation can be greatly aided by ascertaining whether a drug might become a drug of abuse during the drug approval process.

The Controlled Substance Act (CSA) was enacted as Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970. The CSA replaced all previous laws that placed restrictions upon controlled substances. Furthermore, the framework within the CSA applied to all controlled substances that would be regulated in the future. As designed, the CSA sought to evaluate individual controlled substances based upon abuse potential, safety, and medical utility (Courtwright, 2004; Griffin, Miller & Khey, 2008; Spillane, 2004). The act divides all controlled substances into five categories, or as they are known within the act, schedules. Schedule I drugs are considered to have a very high abuse potential and no recognized or accepted medical use. Physicians cannot prescribe them except in very rare circumstances. Schedule II drugs have the same very high abuse potential as Schedule I, although they all have an

accepted medical use. Physicians may prescribe them, but regulations are strict. Schedule III drugs are considered to have a high abuse potential and physicians routinely prescribe them. Schedule IV drugs have a moderate abuse potential, an accepted medical use, and physicians routinely prescribe them. Schedule V drugs have a low, but significant abuse potential and an accepted medical use. No prescription is necessary to obtain them. Accurately predicting the abuse liability of a drug can aid in scheduling decisions, satisfies the requirements of the approval process and help in making preparations for potential diversion or misuse of a new drug (Mansbach, Feltner, Gold & Schnoll, 2003).

In 1984 an amendment to the CSA was passed called the Comprehensive Crime Control Act. New drugs were becoming increasingly plentiful and despite the improvements in drug regulation made by the CSA, many worried that the control scheme in place was not able to deal with new substances in a timely manner. The Comprehensive Crime Control Act granted the Administrator of the DEA the authority to a place a drug (either new or previously scheduled) into Schedule I for up to one year on an emergency basis, with one extension of six months to the order. Such a power was intended to temporarily take the substance off the market until the FDA and/or Congress could decide how to act (Gahlinger, 2004).

The earliest measure to determine if a drug might become a drug of abuse (before the drug is given FDA approval) is through the use of animal testing. So long as a comparable animal species is selected to that of humans, studies of drugs using animals as test subjects are able to use a greater variety of doses of the medication, as

well as carry out the testing for longer periods of time (Ator & Griffiths, 2003).[21] One of the problems of assessing abuse liability in human clinical trials is that these trials are primarily concerned with drug safety and efficacy. Additionally, many trials use traditional patients that need the drug for medical purposes and whether they enjoy using a drug (an indicator of potential recreational use) is not given a lot of attention (Brady, Lydiard & Brady, 2003). As Balster and Bigelow (2003) note, the last College on Problems of Drug Dependence report argued "testing should include representatives of 'the population likely to be administered the drug clinically'" (p. S17). They additionally note that many experts within the field argue that drug abusers are "the most appropriate test population" when considering abuse liability assessment. Griffiths, Bigelow and Ator (2003) argue that oversights in abuse liability assessment can be corrected by assessing abuse liability in human subjects (on a volunteer basis) with histories of substance abuse. One shortcoming with such an approach, however, is that human studies are tightly controlled and human volunteers are supposed to take the drug as directed. They are not allowed to alter the drug, such as crushing the drug to snort or inject it. Although such occurrences can be foreseen, these methods of intake or drug alteration cannot be observed in a human clinical trial (Wright, Kramer, Zalman, Smith & Haddox, 2006). Nevertheless, McColl and Sellers (2006) note that recreational drug users in human trials should be screened to confirm that they are not drug dependent or undergoing drug treatment.

One of the most often cited predictors to determine if a new drug will be abused is the formulation of the drug; specifically, if the drug is an immediate-release or

[21] Epstein, Preston and Jasinski (2006) provide a detailed account of how animal testing was used to investigate the potential abuse liability of tramadol.

controlled-release pharmaceutical product. Typically, recreational drug users will prefer CNS drugs that are more quickly absorbed so that a user will be able to obtain a recreational high quicker (Mansbach et al., 2003). As mentioned previously, pharmaceutically manufactured drugs have been abused and/or altered by recreational drug users. If a pharmaceutical company has reason to believe that this might be a problem with a new drug, then the company should consider alterations to the composition of the new product that will deter or eliminate such occurrences. Altering the formulation and making drugs tamper-proof or tamper-resistant can decrease drug misuse (Mansbach et al., 2003; McColl & Sellers, 2006; Sapienza, 2006; Wright et al., 2006).[22]

Abuse liability assessment does not end after a drug is approved and scheduled by the FDA (Arfken & Cicero, 2003). Although the United States has one of the most rigorous and comprehensive testing system for drugs, problems with or associated with a drug can appear after FDA approval is given (Arfken & Cicero, 2003; Hawthorne, 2005). Despite what some observers would call an overcautious drug regulation scheme in the United States, postmarketing surveillance is still relatively new and developing. Postmarketing surveillance is typically limited to reporting institutional surveillance systems (such as the Drug Abuse Warning Network (DAWN)) or public surveys (such as Monitoring the Future or the National Household Survey on Drug Abuse (NHSDA)) (Arfken & Cicero, 2003).

[22] McColl and Sellers (2006) describe five strategies of drug formulation to decrease abuse liability: controlled/delayed/mixed release, tamper resistant drugs, agonist antagonist combinations, pro-drug CYP P450 inhibitor combination and inclusion approaches.

In 1995, the drug tramadol hydrochloride was introduced to the American drug market under the trade name Ultram®. Ultram® is an analgesic that had been sold in Europe since the late 1970s. The manufacturers of Ultram® wanted their drug to be sold without being scheduled. The FDA tentatively granted the request, albeit with the caveat that aggressive postmarketing surveillance be conducted to see if abuse liability concerns would allow Ultram® to be sold as an unscheduled drug. One study contacted monitoring services for health care professionals with substance abuse, mental health and physical disorders. The participants in this study were already required to give urine samples to monitor drug use. Ultram® was added to the list of screened substances to determine if there were indications that it was a drug of abuse (Knisely, Campbell, Dawson & Schnoll, 2002). Another postmarketing study of Ultram® interviewed a "key informant network" comprised of 110 National Institute of Drug Abuse (NIDA) grantees studying drug abusing-populations and 145 other drug abuse experts. These results were compared to reports from the FDA MedWatch reporting system (Cicero et al, 1999). A subsequent postmarketing survey of Ultram® specifically evaluated the veracity of reports of Ultram® abuse to MedWatch (Woody et al, 2003). Other studies have surveyed persons admitted to drug abuse treatment centers to monitor what drugs they are using (Arfken, Schuster & Johanson, 2003; Jaffe et al., 2004).

In some instances a drug may be placed into one schedule of the CSA, but later circumstances have caused the DEA or Congress to reclassify the substance into a schedule with more stringent controls. Two examples of this process occurred with the drugs MDMA and GHB. Methylene-dioxy-methamphetamine (MDMA) was first

synthesized in 1912 by the German pharmaceutical company Merck (Beck & Rosenbaum, 1994; Eisner, 1994; Gahlinger, 2004; Holland, 2001). Although a few tests of the drug were conducted to determine if it had a medical utility, positive results were lacking and the drug was largely forgotten until the 1970s (Eisner, 1994; Gahlinger, 2004). Researchers studied MDMA hoping the drug could help treat a variety of ailments; primarily due to MDMA's somewhat unique status as an empathogen among drugs. Many researchers found it useful in various forms of therapy. However, it was not long before MDMA became popular in recreational drug circles[23] (Beck & Rosenbaum, 1994; Eisner, 1994; Gahlinger, 2004; Holland, 2001). In 1994 the DEA placed MDMA in Schedule I of the CSA. Despite litigation challenging the Schedule I status and an Administrative Judge ruling that MDMA was a better fit in Schedule III, the DEA was able to keep MDMA in Schedule I and the only governmental authority that could seemingly change such a decision (the United States Congress) took no action to stop the order. Such an action (the placement of MDMA into Schedule I) effectively made it impossible for researchers to continue experiments with the drug[24] (Eisner, 1994).

Gamma-hydroxybutyrate (GHB) was first developed as a sedative/hypnotic and anesthetic. It was used in Europe for these purposes, but not in the United States (Gahlinger, 2004; Nicholson & Balster, 2001). GHB became popular in the United States among people in the bodybuilding community. The drug caused a deep sleep that many believed would provide them a better opportunity to heal after long workouts

[23] Especially among participants at raves.

[24] For a discussion of the consequences of scheduling on drug research see (Doblin, 2000; Jaffe, 1985; Griffin, 2011).

(Gahlinger, 2004; Nicholson & Balster, 2001). Abuse liability assessment tests in animals showed a low likelihood of the drug being a substance of abuse (Nicholson & Balster, 2001). This changed when reports started to circulate that not only were people using it recreationally as an alcohol substitute, but it was being used to facilitate sexual assaults and "date rapes" (Gahlinger, 2004; Griffin, 2011; Nicholson & Balster, 2001). Due to this reputation, GHB was placed into Schedule I by the Hillory J. Farias and Samantha Reid Date-Rape Prohibition Act of 2000, a law signed by President William J. Clinton on February 18th of that year (Gahlinger, 2004; Griffin, 2011).

In the cases of MDMA and GHB, the abuse liability system failed to account for subsequent social contexts of their use. However, in some cases the formulation of a drug might itself be susceptible to alterations of the drug by consumers, alterations which may then lead to harms suffered by the user. In 1967 pentazocine, marketed under the trade name Talwin®, was given FDA approval (Baum, Hsu & Nelson, 1987). The drug, a non-narcotic analgesic, was not known as a drug abuse and in the immediate following years misuse was confined to small numbers of people within the medical community. Beginning in the late 1970s though, enterprising drug addicts discovered that dissolving Talwin® tablets with the antihistamine tripelennamine, filtering the solution and injecting it intravenously produced a high similar to using heroin. Such a mixture became known as the "T's and blues."[25] This combination of drugs quickly became a problem (Baum et al., 1987; Poklis, 1983; Showalter, 1980). In 1981, Sterling-Winthrop (now Winthrop Breon) met with FDA officials to discuss possible solutions to the problem. The company agreed to pull Talwin® from the

[25] Baum et al. (1987) note that tripelennamine tablets were typically blue. Thus, "T" being short for Talwin® in combination with blue tablets produced the moniker.

pharmaceutical market and in 1982 was given FDA approval for the drug Talwin Nx®. This new formulation of the drug added .5 milligrams of naloxone HCl (a narcotic antagonist) to pentazocine. When taken as directed, the naloxone had no affect on the medication. However, when the medication was crushed and injected, the naloxone blocked most of the euphoric high previously experienced. This change in formulation effectively ended the T's and blues "epidemic"[26] (Baum et al., 1987; Poklis, 1983).

One common impediment to regulation within the pharmaceutical industry is off-label use. As previously mentioned, in order for a company to obtain approval for a new drug, there must be strong evidence that demonstrates safe use as well as its ability to alleviate or treat a medical condition. A pharmaceutical company may advertise their drug based upon these recognized uses, however, doctors are not limited to these uses when prescribing drugs. The FDA regulates the approval of drugs, not the practice of medicine. Unless state laws or medical boards state otherwise, doctors are able to prescribe drugs as they see fit. Although pharmaceutical companies are prohibited from advertising for off-label use, there are ways they can inform doctors of alternative uses for the drugs they sell. Pharmaceutical companies will have their salespeople inform them of alternative uses during site visits, conferences or paid "junkets", or pharmaceutical salespeople will provide copies of journal articles documenting successful alternative uses for the drugs they sell (Hawthorne, 2005).

Although off-label use is common, perhaps one of the more ironic occurrences in pharmaceutical regulation concerns the previously vilified drug Thalidomide.

[26] Poklis (1983) noted there was a shortage of heroin during the peak years of T's and blues use. This shortage most likely exacerbated the problem by sending opiate users in search of newer and more accessible forms of opiates.

Thalidomide has become synonymous with dangerous drugs and was responsible for one of the worst human tragedies associated with pharmaceuticals. Thus, it would probably surprise many that thalidomide was given FDA approval in 1998. As mentioned previously, the side effects that could be caused by thalidomide were not properly investigated before the drug was introduced to the pharmaceutical market in many countries. Foremost among these side effects was that pregnant women should never take the drug. In the 1960s, a doctor in Israel needed a sedative for patients with leprosy. Among this class of patients, pregnancy was not a concern and the doctor chose to give them thalidomide. After prescribing thalidomide to these patients, the doctor noticed that it treated a certain type of lesion, as well as nerve deterioration. Familiar with this research, an immunologist in New York later discovered that thalidomide appeared to inhibit the growth of a protein which produces immune cells and inflammation within humans. Therefore, thalidomide could potentially be used to treat the symptoms of a plethora of diseases such as: rheumatoid arthritis, tuberculosis, Crohn's disease, cancer-related weight loss and AIDS (Hawthorne, 2005).

Although it appeared that thalidomide could potentially have several needed medical applications, the stigma associated with the drug was so strong that pharmaceutical companies were reluctant to attempt to market or sell thalidomide. Thalidomide lacked FDA approval and it was virtually assured that this would not be given easily, or at least that was the conventional thinking of most pharmaceutical companies. The FDA, however, had somewhat of a problem on their hands. Among public interest groups, AIDS activists have a lot of political clout and are extremely vocal. Since the discovery of the disease, the FDA has been repeatedly accused of

needlessly delaying many potential AIDS medications while AIDS patients were continually dying. AIDS activists and patients were aware of the potential thalidomide had and were starting to smuggle the drug from Brazil, where leprosy is a more common disease than in the United States. Indeed, in the United States leprosy rarely occurs. The FDA was sympathetic to AIDS patients (as well as people with other diseases that could potentially benefit from thalidomide), but knew that if proper regulations were followed FDA approval would take years. In the mean time thalidomide was being smuggled into United States and the FDA was unable to regulate it. The credibility of the FDA, in many ways, seemed to be at stake (Hawthorne, 2005).

In 1994, the FDA requested a meeting with Celgene, the pharmaceutical company that would market thalidomide in the United States. After the meeting, the FDA informed Celgene that they would allow the corporation to do a retrospective study of twenty years of thalidomide use by leprosy patients in the Hansen's Disease Center in Louisiana. Such an accommodation to a pharmaceutical company is extremely rare. Eventually thalidomide was given FDA approval for the treatment of leprosy, however, Celgene and the FDA first completed the System for Thalidomide Education and Prescription Safety (STEPS) program. The program provided various safeguards to make sure that pregnant women did not take the drug (Hawthorne, 2005).

Hawthorne (2005) notes that nearly half the prescription drugs taken in the United States are administered off-label. The FDA does not have the resources or the authority to completely stop this practice; however, there are many instances where the FDA would not want to stop this practice. That the FDA would design a safe-guarding program for the use of a prescription drug, that is clearly for a different use than it was

given approval, can have troubling consequences. Although such a position could be viewed as harm reduction, it also can be viewed as approving non-recommended use of pharmaceuticals. Celgene could have submitted an application for additional approved usages of thalidomide, but the corporation had no need to. As mentioned earlier, there are many ways a pharmaceutical company can let physicians know about other uses for their drugs besides traditional advertising. All Celgene needed (or any other pharmaceutical company needs) is a single FDA approved use.

Pharmaceutical Advertising

One of the most ubiquitous criticisms of Purdue Pharma has centered around their advertisement and marketing of OxyContin® (Inciardi & Goode, 2003; Van Zee, 2009). According to Singh (2007) "Drug advertisements are an important part of a drug company's persuasive arsenal" (p. 133). Many doctors and potential consumers of pharmaceutical products receive the majority of their information about these products via the advertisements of the companies that are selling them. These practices have not only led to more doctors prescribing drugs, but patients asking to be prescribed prescription drugs (Singh, 2007). Considering that many rely on advertising for information and that certain drugs could potentially be harmful, determining the efficacy and accuracy within advertising is paramount to protect consumers. Braithwaite (1993) argues that misrepresentations by pharmaceutical companies can have serious consequences.

As Sutherland indicated, one of the most scrutinized practices of the pharmaceutical industry is their advertising practices (Sutherland, 1940, 1983). Early studies focused on the amount of direct-mail advertisements sent to physicians. These

studies measured how often physicians actually opened unsolicited advertisements, as well as how often these advertisements are actually read. Additional concerns were the efficacy of direct-mail to physicians versus advertisements in medical journals (Belley, 1943; Chandra & Holt, 1999; Ferber & Wales, 1958; Fisher, 1991; Jeuck, 1940; Parker & Pettijohn, 2003; Rand, 1941; Wegner, 1960). Another study sought to understand the biggest influences on the selection of certain pharmaceutical products by physicians. Pharmaceutical salespeople (31.1%), direct-mail (15.6%) and journal advertising (5.6%) compromised 52.3 % of the introductions of physicians to new products. Journal articles (18.8%), colleagues (14%), conferences (5.2%), other sources (4.2%), patients (2.9%), conventions (2.3%), and druggists (.3%) were the remaining categories (Caplow & Raymond, 1954). Wegner (1960) noted that from 1953 to 1958 pharmaceutical advertisement pages per journal increased by thirty-four percent.

Simon & Eitzen (1990) argue there is a fundamental problem with advertising; it is specifically designed to be deceptive. According to them, advertising is designed to manipulate. Deception in advertising typically occurs in two ways: blatantly false advertising and puffery. In 1978, the Federal Trade Commission cited American Home Products, the maker of the drug Anacin, for false advertising. Prominent among several false claims was that Anacin was “A Better Aspirin Formula,” when in fact one tablet of Anacin merely contained twenty-three percent more aspirin than a regular aspirin tablet and the same amount of caffeine as one-third a cup of coffee. Simon and Eitzen identify puffery as such ubiquitous advertising slogans as “Nestle makes the very best chocolate” or “Coke is it.” Additional problems with false advertising have arisen with the relatively recent phenomenon of pharmaceutical advertising direct to consumers

(Wilkes, Bell & Kravitz, 2000; Berndt, 2005; Chandra & Holt, 1999; Holmer, 1999; Mintzes et al., 2002; Parker & Pettijohn, 2003; Pinto, 2000; Handlin, Mosca, Forgione & Pitta, 2003). These expenditures have increased dramatically over the last twenty years (Handlin et al., 2003; Parker & Pettijohn, 2003; Pinto, 2000). Pinto (2000) has speculated that pharmaceutical advertising to consumers will eventually surpass technological, fast food and soft-drink advertising. Additional concerns are promotions, gifts and kickbacks from pharmaceutical companies to physicians (Dresser, 2006; Parker & Pettijohn, 2003; Sismondo, 2004).

Not only can advertising promote and sell a drug, advertising can provide a new image to older medications and tout new uses for these drugs. Methylphenidate, better known by the trade name Ritalin, was introduced to the U.S. drug market in 1957. Yet, many perceive of the drug as relatively new due to its widespread promotion beginning in the 1980s. Although researchers have given stimulants to children with behavioral problems since the 1920s, the growing recognition of conditions such as Attention Deficit/Hyperactivity Disorder (ADHD) has provided pharmaceutical companies additional opportunities to market and sell drugs (Singh, 2007).

Drug regulation evolved a great deal during the twentieth century. The century began with the passage of a law that only required that pharmaceutical companies merely provide labels that truthfully listed what ingredients were included in a medication. The Pure Food and Drug Act of 1906 was certainly a positive legislative development at the time, however, the government lacked the means to enforce the act. Additionally, despite the requirement that pharmaceutical companies accurately label their products, pharmaceutical companies did not have to prove that their products were

safe or actually worked. Although it required the tragic experiences with the drugs sulfanilamide and thalidomide to give the government the rationale and moral authority, the drug regulation apparatus would eventually evolve to the point where it required both that a drug was safe for use and effective before a pharmaceutical product was allowed to reach the American drug market. In addition to premarket scrutiny, postmarket surveillance of drugs has been created and continues to evolve. Several government reporting services now track the use and abuse patterns of drugs after these substances reach the drug market. Granted, the FDA is dependent on pharmaceutical companies to fund and carry out tests that demonstrate drug safety and efficacy, to gain approval for a drug the FDA must be presented with this data in a clear and comprehensive manner. If the FDA was shouldered with this duty, the agency would require a drastic increase in funding and the process of drug approval would be lengthened considerably. Considering the pecuniary commitment from American taxpayers such a drug control scheme would require to give the FDA the resources to test pharmaceutical products is probably untenable. Furthermore, considering the complaints voiced by many that the drug approval process is too lengthy already; few would encourage or support a system change that would lengthen the drug approval process.

CHAPTER 4
OXYCONTIN® AND THE PROBLEM OF PAIN

OxyContin® was introduced to the American drug market in 1996 as a Schedule II substance (Inciardi and Goode, 2003; Van Zee, 2009). Despite a patent being granted to Purdue Pharma in 1995, the medication was not necessarily new. Indeed, the active ingredient in OxyContin® (oxycodone) has been used for nearly one hundred years. Oxycodone is a highly effective drug for the management of pain, especially for moderate to severe pain caused by chronic pain or terminal cancers. Examples of other brands of medication that contain oxycodone as the active ingredient include: Percocet® (oxycodone and acetaminophen), Percodan® (oxycodone and aspirin), Roxicet® (oxycodone and acetaminophen), Roxicodone® (oxycodone), Endocet® (oxycodone and acetaminophen), OxyIR® (oxycodone), and Tylox® (oxycodone and acetaminophen) (Inciardi and Goode, 2003). This chapter will begin by tracing the development of opiates, their efficacy as painkillers and how this process led to the development of OxyContin®. Both the efficacy of OxyContin® and how it became so widely abused will be discussed. Finally, the details of the settlement to a criminal investigation between Purdue Pharma and the government will be discussed.

Origins and Efficacy

The oldest problem in medicine is the treatment of pain, yet the treatment of this malady has not changed much until recently. Throughout human history, the most common and effective remedy for the treatment of pain has been opium. Although alleviating a patient's medical condition with the treatment of medicine might seem like a process which should not illicit much debate, the treatment of pain is not that simple. The root causes of pain have historically been poorly understood and pain is often

viewed as a natural part of the human experience. Therefore, treating a natural malady that often defines humanity with a drug considered dangerous and addictive has been and continues to be a problem (Meldrum, 2003). Hippocrates believed opium should be used in moderation. Two ancient Greeks, Erasistratus and Diagoras of Melos, living in the fifth and third centuries B.C. respectively, argued it was better to suffer pain than become dependent upon opium (Booth, 1996).

The first known references to the utilization of opium for the treatment of pain are found in the texts of ancient Sumeria, one of the world's oldest known civilizations. Not only was opium used for the treatment of pain, but texts such as the Thebes papyrus of 1552 B.C. recommend the use of opium for over 700 ailments. Opium, however, was not just for medicinal purposes. Initiates of the cult of Demeter revered the plant and statues of the goddess often showed her holding a poppy plant. The ancient Greeks and Romans associated opium with both sleep and death. An overdose of the drug was viewed as an honorable means of suicide. Hannibal of Carthage kept a lethal dose of opium in his ring. He used it when he took his own life in 183 B.C. Opium has also been abused in smokable form, a practice often associated with the Far East, but practiced in many other countries as well (Booth, 1996).

The first alteration of opium was to merely make the drug more appetizing to patients. To mask the extremely bitter taste of opium, many mixed the drug with honey, nutmeg, cardamom, cinnamon and other spices. In 1524, the Swiss physician Paracelsus returned from Constantinople to Western Europe with a concoction he called laudanum, a tincture of opium mixed in alcohol. It would be used for the

treatment of almost every ailment and for recreational purposes as well (Gahlinger, 2004).

Morphine, the active principle of opium, was first isolated in 1803. Morphine has ten times the strength of crude opium as a painkiller. The invention of the hypodermic needle in 1848 greatly aided the administration of morphine for the treatment of pain, however, it was soon noted that morphine was highly addictive. Ever since, researchers and physicians have sought to find an opiate with the greatest potential as a pain killer, but with the lowest addictive properties. In 1832, researchers found another natural component of opium, albeit less effective as a painkiller than morphine and with less potential for addiction or abuse. This compound was given the name codeine. In the coming years, researchers began to develop semi-synthetic derivatives of opium. Examples of these derivatives are: diacetylmorphine, oxycodone, hydrocodone and hydromorphone to name a few (Gahlinger, 2004).

Although several researchers had synthesized and written about diacetylmorphine, a combination of morphine and acetic acid, it was not until 1898 that the drug was available for purchase. The German pharmaceutical manufacturer Bayer Laboratories, observing diacetylmorphine was a more powerful painkiller than morphine, wanted a trade name befitting the new drug. Heinrich Dreser, the chemist that had produced the drug, decided to name it heroin after the German word heroisch, which meant mighty or heroic (Booth, 1996). Not only was heroin a more powerful painkiller than morphine, it was initially believed heroin was less addictive than morphine as well and Bayer marketed the drug accordingly. However, this notion was quickly dispelled and heroin has become known as one of the most addictive and destructive drugs ever

produced. Heroin was controlled by the Harrison Narcotic Act of 1914 and eventually banned for use in the United States in 1920 (Courtwright, 1982; Gahlinger, 2004; Goode, 1999; Musto, 1999). Thus, a drug that was believed to be and marketed as less addictive turned out to be more dangerous than the substance it was supposed to replace. Critics of OxyContin® have often compared the drug to heroin based upon abuse potential; knowledge of the history of heroin further buttresses this comparison.

Treating patients who abuse or are addicted to opiates has been problematic (Acker, 2002; Courtwright, 1982; Musto, 1999; Gahlinger, 2004; Goode, 1999). This experience has led both government agencies responsible for promoting health and controlling drugs as well as pharmaceutical companies to research and hopefully discover analgesics with low abuse potential. If drugs such as these could be found, it has been hoped by many that morphine could eventually be eliminated from the American pharmacopeia. Realizing this goal, and a few others previously mentioned, led to the establishment of the Committee of Drug Addictions and many other bureaucratic agencies to promote addiction research; both to promote a better understanding of addiction and drugs that may cause it (Acker, 2002).

Opiates, since the invention of the hypodermic syringe, have been traditionally administered via intravenous injection. This method has provided quicker and more effective pain relief than via oral administration. As Thirlwell et al. (1989) note, in the 1960s, it was believed that oral morphine had approximately one-sixth the potency as morphine delivered via intramuscular injection. Additionally, one study noted that oral morphine was metabolized by the body so rapidly that only a fraction of the medication was utilized by the body for the alleviation of pain. Such a conclusion led many within

North America to believe that morphine was not an effective analgesic when administered orally. Beginning in the 1970s, studies in the United Kingdom and Canada found when oral morphine was administered regularly in individually titrated doses; the medicine could be effective in controlling pain in cancer patients (Melzack, Ofiesh, & Mount, 1976; Melzack, Mount & Gordon, 1979; Saunders & Baines, 1983; Twycross, 1974).[27] After further study, it was also found the injection versus oral administration ratio was actually closer to a 1:2 or 1:3 ratio of efficacy rather than 1:6, as was previously believed (Thirlwell et al., 1989).

Although physicians began to utilize oral morphine for the treatment of severe cancer pain, its short half-life (usually about two to three hours) posed some problems. Patients required doses every four hours in order to receive the most effective pain relief, meaning the medication often failed to allow patients to be able to sleep through the night. MS Contin®, introduced to the American drug market in 1984, was one of the first answers to the dosing problems associated with oral morphine. The drug was the first controlled release morphine in a pill form. Thirlwell et al. (1989) found MS Contin® was effective over a twelve hour dosing period and had minimal side effects.[28] Studies showed pain medications using a Contin release system provided extended duration of pain relief, more constant plasma concentrations and clinical effects and fewer side effects. Studies also noted at the time the potential problems with time release preparations like MS Contin®, including problems with the drug being released either too slowly or too rapidly.

[27] In a 1983 article Walsh (1983) addresses what he refers to as eleven common misunderstandings about the use of oral morphine for the treatment of pain.

[28] The study by Thirlwell et al. (1989) was funded by a grant from Purdue Frederick, Inc., Toronto, Ontario, Canada.

One problem in studying controlled-release morphine is the patient population. As Hanks (1989) notes, few randomized, double-blind controlled studies had been conducted of MS Continus[29] due to the different symptoms and considerations that have to be given to individual patients. Despite this, most of those that were eligible to receive the medication indicated that the controlled-release was effective. One qualification given though is that some prefer immediate-release formulations of morphine when introducing the medication to new patients. After the patient has been stabilized, a controlled-release morphine can be safely introduced to the patient. Levy (1996) notes that controlled-release morphine became a heavily utilized drug because of the ease of administration and titration.

Morphine was thought to be a more powerful drug than oxycodone; however, oxycodone appeared to have fewer side effects. Studies showed morphine caused more instances of nausea and some people taking morphine have been known to see hallucinations (Kalso & Vainio, 1990; Kantor, Hopper, & Laska, 1981; Poyhia, Vainio & Kalso, 1993). The abuse liability of oxycodone, including risk of developing dependency, is similar to morphine (Eddy, Halbach & Braenden, 1956; Poyhia et al., 1993). According to the original warnings from the manufacturer of Percodan®, "The habit-forming potentialities of Percodan approach those of morphine more closely than those of codeine. The same care should therefore be exercised when using Percodan as when morphine is prescribed" (Bloomquist, 1963, p. 127). Studies have shown, however, when taken orally oxycodone is twice as effective to similar doses of oral morphine Beaver, Wallenstein, Rogers & Houde, 1978; Bruera et al., 1998; Hagen &

[29] As it is known in the United Kingdom.

Babul, 1997; Sunshine et al., 1996). Additionally, studies have shown the use of oxycodone carries with it less social stigma than morphine. Morphine is viewed by many people as a highly addictive substance typically taken by people close to or awaiting death (Glare & Walsh, 1993; Kalso & Vaino, 1990; Levy, 1996, 2001b). The only side effect oxycodone seems to have at a greater rate than morphine is constipation. The most common side effects of oxycodone are drowsiness, lightheadedness, nausea, vomiting, pruritis, constipation and sweating accompanied by hot flashes (Davis, Varga, Dickerson, Walsh, LeGrand & Lagman, 2003). When conducting a meta-analysis of six studies that covered 160 patients Reid, Martin, Sterne, Davies & Hanks (2006) found oxycodone was comparable to similar medications, but not definitively better.

Until the introduction of OxyContin®, oxycodone has only been available in dosages suitable to relieve minor pain. This made it unsuitable to treat severe or chronic pain (Glare & Walsh, 1993; Rodgers, 1991). Formulations of the drug were typically in five milligram doses with a combination of a nonopioid analgesic. Examples of such a combination are Percocet® (which contains oxycodone and acetaminophen) and Percodan® (which contains oxycodone and aspirin) (Glare & Walsh, 1993). As a result of these mixtures, no more than two tablets could be taken every four hours to prevent hepatotoxicity (damage to the liver) from excess acetaminophen or salicylism (a toxic dose of salicylic acid) and gastrointestinal intolerance from excess aspirin (Glare & Walsh, 1993; Levy, 1996). To treat moderate to severe pain, therefore, a single-entity oxycodone is required. In one study it was found that Roxicodone in up to sixty

milligram dosages in patients was safe, effective and acceptable as an analgesic (Glare & Walsh, 1993).[30]

Early scientific tests of OxyContin® demonstrated the efficacy of the drug. In one of the first studies on controlled-release oxycodone, one group was given three five milligrams of immediate-release oxycodone tablets (Roxicodone®), one group was given one, two, or three ten milligrams of controlled-release oxycodone tablets (OxyContin®) one group was given two tablets containing five milligrams immediate-release oxycodone and acetaminophen 325 milligrams (Percocet®) and one group was given placebo pills. The study found patients who had taken all three doses of controlled-release oxycodone experienced pain relief throughout a twelve hour period, while the two immediate-release forms of oxycodone experienced six to eight hours of pain relief. Pain relief during these time periods were comparable and the only benefit of an immediate-release oxycodone was the drug worked about five minutes faster, which the researchers stated was not clinically meaningful (Sunshine et al., 1996).[31]

Parris et al. (1998) had similar findings to Sunshine et al. (1996) when comparing OxyContin® and Roxicodone®. Hagen & Babul (1997) found controlled-release oxycodone (OxyContin®) was comparable to controlled-release hydromorphone (Hydromorph Contin®). Bruera et al. (1998) found OxyContin® was at least effective as MS Contin® in treating cancer pain.[32][33] Mucci-LoRusso et al. (1998) had similar

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[30] The study by Glare and Walsh (1993) was supported by Roxane Laboratories, Columbus, Ohio.

[31] The study by Sunshine et al. (1996) was supported by a grant from The Purdue Frederick Company, Norwalk, Connecticut.

[32] Keeping in mind the 2:1 ratio of oxycodone to morphine when taken orally.

[33] One of the authors of Bruera et al. (1998) is listed as an employee of Purdue Frederick.

findings to Bruera et al. (1998) with the additional observations that patients using OxyContin® did not hallucinate (two cases with MS Contin®) and patients using OxyContin® did not suffer from pruritis in as many cases as those who had taken MS Contin®. Otherwise, side-effects between the two drugs were comparable.[3435]

Caldwell et al. (1999) found controlled-release oxycodone and oxycodone with acetaminophen, when used by patients with osteoarthritis, provided comparable pain control and sleep quality. Additionally, they found controlled-release oxycodone was associated with fewer side-effects.[36] Roth et al. (2000) found patients suffering from osteoarthritis-related pain that took twenty milligram OxyContin®, instead of placebo, experienced less interference of pain with mood, sleep and enjoyment of life. Common opioid side effects were reported and the medication seemed to be effective and safe for patients with chronic, moderate to severe, osteoarthritis-related pain.[37] Watson & Babul (1998) found that compared with placebo, OxyContin® was an effective analgesic for the management of steady pain, paroxysmal spontaneous pain, and allodynia, all symptoms of postherpetic neuralgia (a complication of shingles that is often characterized by burning, aching, or itching with few effective treatments).[38] Hale et al. (1999) found that patients with chronic back pain that could not be adequately treated by non-opioid medications, experienced comparable pain-relief and similar side-effects when taking controlled-release oxycodone as those that took immediate-release

[34] Keeping in mind the 2:1 ratio of oxycodone to morphine when taken orally.

[35] One of the authors of Mucci-LoRusso (1998) is listed as an employee of Purdue Frederick.

[36] Caldwell et al. (1999) was sponsored by Purdue Pharma.

[37] Roth et al. (2000) was sponsored by Purdue Pharma.

[38] Watson & Babul (1998) was sponsored by Purdue Pharma.

oxycodone.[39] Watson, Moulin, Watt-Watson, Gordon & Eisenhoffer (2003) found that OxyContin® resulted in less pain and a better quality of life over placebo in patients with diabetes mellitus.[40]

Researchers had determined that OxyContin® could effectively treat pain in a manner comparable to intravenous morphine injection; the time release capsule required fewer doses than other oral medications and produced fewer side effects than morphine. However, another way to compare and evaluate drugs is based upon the cost of the medication. Certain critics of OxyContin® argued the medication might be better than oxycodone in immediate-release form, but considering the high cost of each dose of OxyContin® compared to an equivalent amount of immediate-release oxycodone, prescribing OxyContin® was not cost effective. From 1999-2001 Liberty Northwest Insurance Company in Portland, Oregon experienced a great surge in expenses. This increase in expenses was largely a result of increased pharmacy costs associated with controlled-release oxycodone (Rischitelli & Karbowicz, 2002). Increases in sales of controlled-release oxycodone have led to increased spending on Medicaid patients as well (Davis et al., 2003). Rischitelli & Karbowicz (2002) conducted a study of sixteen clinical trials that compared controlled-release oxycodone to immediate-release, controlled-release morphine, and methadone. The researchers found that in most cases[41], there was no difference between the medications other than the number of doses that needed to be taken. Although a person would have to take

[39] Hale et al. (1999) was sponsored by Purdue Pharma.

[40] One of the authors of Watson et al. (2003) was employed by Purdue Pharma.

[41] One study comparing controlled-release oxycodone to immediate-release oxycodone showed the controlled-release had fewer side-effects.

more pills with the immediate-release oxycodone, the cost of those pills was less than a comparable number of controlled-release pills. The researchers noted that considering the differential doses required for MS Contin® and OxyContin®, cost comparisons could not easily be made. The researchers note that OxyContin® should be available for those who experience side-effects which prevent them from taking other medications, but for those that do not, there are cheaper options (Rischitelli & Karbowicz, 2002).

A Developing Problem?

The very thing that set OxyContin® apart, that it delivered oxycodone via a time release capsule, also became the basis for its widespread abuse. One dose of OxyContin® worked for twelve hours versus four hours for other medications, but it did not take long for people to figure out that crushing the time release capsule would allow a person to take a much stronger immediate dose which would lead to a very strong and euphoric high (Cicero, Inciardi & Munoz, 2005; Inciardi & Goode, 2003; Sees, Di Marino, Ruediger, Sweeney & Shiffman, 2005; Tunnell, 2005; Van Zee, 2009). As Van Zee (2009) notes, Purdue Pharma's own testing in 1995 showed that the crushing of the time release capsule allowed for up to sixty-eight percent of the oxycodone in OxyContin® to be ingested immediately.

Reports of OxyContin® abuse and diversion first surfaced in southern Maine and then spread to several other states. Many of these states were in Appalachia or rural areas within the United States (Cicero et al., 2005; Inciardi & Goode, 2003; Tunnell, 2005). As Inciardi and Goode (2003) note, because of the rural nature of these communities, illegal drug markets do not typically extend into these areas. Therefore, many rely upon prescription drugs in lieu of more traditional street-drugs that people

might typically abuse. According to Tunnell (2005) OxyContin® diversion typically occurs by fraudulent prescriptions, illegal sales, pharmacy theft, doctor shopping, foreign diversion, and through family members or friends that have valid prescriptions. The Drug Enforcement Administration (DEA) reported that from 2000 to 2001, there was a seventy-five percent increase in property and other crimes associated with OxyContin® alone. In this same time period, OxyContin® arrests increased by sixty-seven percent (DEA, 2002). Thefts of OxyContin® at pharmacies led many to not only stop dispensing the medication, but advertise on storefront windows of this policy as a deterrent to potential thieves (Tunnell, 2005; Ukens, 2001).

In 2001, first quarter sales of OxyContin® increased by $1,000,000 in just a single one of the company's sales territories (one that included Myrtle Beach, South Carolina). The next largest increase in any other sales territory in the nation was $700,000. This occurred while Purdue Pharma was engaged in a national advertising campaign in which the company was trying to convince the American public they were committed to fighting illicit OxyContin® abuse. Although Purdue Pharma was not specifically required to, the DEA stated that the company should have investigated the disparate sales figures. Indeed, local pharmacies within the sales territory reportedly told Purdue Pharma salespersons about their suspicions of an increase in illicit use after a number of burglaries involving the theft of OxyContin®. Former U.S. Congressman James C. Greenwood noted that companies that sold narcotics should monitor their sales figures for patterns of abuse (Meier, 2001).

Similar suspicions arose around the Comprehensive Care and Pain Management Center in South Carolina.[42] According to pharmacists in the area, the rates of prescriptions from the facility were much higher than other medical facilities.[43] Indeed, law enforcement noted that the lax prescription practices of Comprehensive Care were so well known that "people arrived by the carload from more than 100 miles away" (Meier, 2001, p. 16). Additionally, several pharmacists also told Purdue Pharma salespersons that OxyContin® was being diverted to illicit markets. Executives of Purdue Pharma stated that they did not have prescription data from these pharmacies and thus were not alerted to the problem (Meier, 2001).

To say that OxyContin® was a success for Purdue Pharma would be a tremendous understatement. In 1996 sales of the drug were $48 million. In 2000, OxyContin® sales reached nearly $1.1 billion (Van Zee, 2009). In that same time period prescription rates increased twenty times over. Notable among these sales figures was an increase of OxyContin® sales by forty-one percent between 2000 and 2001 (Inciardi & Goode, 2003). Although these sales figures were no doubt in part due to the efficacy of OxyContin® for the purpose of pain management, Purdue Pharma also marketed the drug aggressively.[44] During the time period of 1996-2001, Purdue Pharma held more than forty conferences at vacation resorts with more than 5,000

[42] Libby (2008) argues that wrongdoing surrounding many pain clinics were overly sensationalized by the media and the product of overambitious prosecutors and Drug Enforcement Administration (DEA) agents persecuting respectable physicians for not being able to determine if patients were doctor-shopping or legitimate pain cases. He further argues that the main push to crack down on prescription drugs was a way to distract the country from the failing war on illegal drugs. Jung and Reidenberg (2007) and Reidenberg and Willis (2007) have drawn similar conclusions.

[43] Considering the clinic specialized in pain management this should not have been a surprise though.

[44] Although pharmaceutical advertisements are no doubt more visible in contemporary times, such tactics have been around since the birth of the industry (Courtwright, 2001; Spillane, 2000).

physicians, pharmacists, and nurses in attendance. All expenses were paid by the corporation. Physicians with high prescription rates of opioids were specifically targeted for direct advertisements via databases that tracked such prescription patterns. Furthermore, Purdue Pharma more than doubled the number of sales representatives promoting OxyContin® and offered huge bonuses for those representatives that managed to increase sales of the drug within their sales district (Van Zee, 2009).

The Settlement

On May 10, 2007 Purdue Pharma pleaded guilty to a felony charge of illegally misbranding OxyContin® in an effort to mislead and defraud physicians.[45] The corporation agreed to pay a $470 million fine to the federal government and provide $130 million to settle personal injury claims (Johnson, 2007). Merely a week before the settlement, Purdue Pharma had boasted on its website that the company was "65-0" against tort claims relating to claimed injuries from OxyContin® (Hammack, 2007). The Commonwealth of Virginia received $5.3 million to fund health care fraud investigations and $20 million for a prescription drug monitoring system[46] (Johnson, 2007). In addition to the guilty plea by the corporation, Chief Executive Michael Friedman, Chief Legal Officer Howard Udell, and former head of research Paul D. Goldenheim pleaded guilty to a misdemeanor count each of misbranding OxyContin®.[47] Each person agreed to

[45] Purdue Pharma specifically pleaded guilty to a felony count of misbranding a drug, with the intent to defraud or mislead, in violation of Title 21, United States Code, Sections 331(a) (which prohibits the introduction or delivery for introduction into interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded).

[46] Several other states received varying amounts from the settlement as well.

[47] The three executives pleaded guilty to a strict liability misdemeanor count, which did not require an intent to mislead or defraud.

three years supervised probation, 400 hours of community service and were required to collectively pay $34.5 million in criminal fines (Brownlee, 2007).

The settlement ended a five year joint federal and state investigation coordinated through the United States Attorney's Office for the Western District of Virginia. Brownlee (2007) noted that Purdue Pharma began using focus groups of primary care physicians in 1995. The purpose of those focus groups was to determine if physicians would be willing to prescribe OxyContin® to patients who suffered from pain that was not caused by cancer. The physicians from these focus groups requested a pain medication that was long-lasting with lower potential for addiction and diversion than drugs that were on the market at that time.

Reaction to the settlement has been mixed. At the Senate Judiciary Committee hearings Senators Leahy and Specter specifically questioned John Brownlee, the U.S. Attorney that had coordinated the Purdue Pharma case, as to why the three executives that pleaded guilty were not required to spend any time in jail or prison (Leahy, 2007; Specter, 2007). Senator Specter even mentioned "Where someone places a dangerous instrumentality in commerce with reason to believe that a death may occur, and a death does occur, that constitutes malice and supports a prosecution for murder in the second degree" (Specter, 2007). Senator Coburn, a practicing physician, expressed concern about the hearings. As he noted, ninety-eight percent of those who had died from OxyContin® were polydrug abusers and that OxyContin® was a small part of a much larger problem (Coburn, 2007). Dr. James Campbell, a witness at the hearings, took a slightly different tact. He noted that since OxyContin® is labeled as a Schedule II drug, and according to that label, has a significant risk for abuse. Therefore, many physicians

should have already been warned to the potential dangers the medicine they were prescribing carried (Campbell, 2007).

The OxyContin® Narratives: Corporate Greed or Moral Panic?

OxyContin® did not materialize out of the abyss. The active ingredient (oxycodone) has been around for nearly a century and OxyContin® was the second drug from the same pharmaceutical company (Purdue Pharma) to feature a narcotic analgesic delivered via a time-release capsule. OxyContin® was not the first legal drug to be widely abused and it is doubtful it will be the last. It has joined a small group of drugs that have been lauded as greatly as they have been vilified. Morphine was viewed as a miracle drug during the American Civil War. Many wounded soldiers would not have survived the pain incurred during surgeries, especially considering the amateurish nature of the practice of medicine at the time. Yet, morphine addiction became so prevalent during the war it became known as the "soldier's disease" (Gahlinger, 2004). Cocaine was originally touted as a miracle drug. Soon afterwards it was portrayed as a menace that turned abusers into "fiends" (Musto, 1999; Spillane, 2000). Such a dichotomy has already occurred with OxyContin®. This dichotomy is best summarized by two different books that discuss the impact of the drug: Barry Meier's *Pain Killer: A "Wonder" Drug's Trail of Addiction and Death* and Ronald T. Libby's *The Criminalization of Medicine: America's War on Doctors*.

Meier (2003) argues OxyContin®, which is a valuable tool in fighting chronic pain, was introduced at a time when new medications were needed, but was introduced to the American drug market when gaps in regulation allowed the drug to become widely abused. According to Meier, Purdue Pharma already had an effective and

successful medication available (MS-Contin®), but the patent was expiring and Purdue Pharma wanted to replace the drug headed to generic status with a new drug (OxyContin®) so the company could continue to reap huge profits. This problem was exacerbated by an unscrupulous company (Purdue Pharma) that marketed the drug to countless physicians who were not pain management specialists or oncologists and lacked appropriate patients for the medication. This marketing campaign was unprecedented for a Schedule II narcotic and led many physicians to prescribe OxyContin® to patients who did not need a medication so powerful and potentially addictive. Meier argued such behavior on the part of Purdue Pharma was not unanticipated. He recounted how the founder of Purdue Pharma, Dr. Arthur Sackler, essentially wrote the book on how a pharmaceutical company can deceive both the American public and government. Sackler trained his brothers Raymond and Mortimer in the family business and they have done the same since Arthur's death.

According to Meier (2003), not only did the FDA fail to anticipate the danger OxyContin® posed, but they unwittingly aided Purdue Pharma by endorsing the company claim the medication had a lower potential for addiction, based upon the belief that drugs delivered via a time release capsule were less desirable to drug users. Meier often portrays the federal regulators as heroic and well-intentioned figures who are ill-prepared and lacking in resources to hold accountable one of the more profitable companies in a notoriously corrupt industry (the pharmaceutical industry). This problem was exacerbated by the fact Purdue Pharma is a privately-owned corporation, since Purdue Pharma does not have to satisfy stockholders, the company is even more secretive than typical pharmaceutical companies. This allowed Purdue Pharma to

obfuscate their role in an American tragedy; thus preventing federal regulators from determining what level of culpability the company had. Both Purdue Pharma and the FDA had knowledge the time release capsule could be easily subverted and this should have delayed the introduction of OxyContin® until a abuse-resistant form of the medication could be available. According to Meier, the ease of subverting the time release capsule and the intensity of OxyContin® made the drug the most sought out prescription drug on the black market ever. This led to crime waves in many rural areas, purportedly caused by addicts either seeking out the drug or committing crimes to obtain the funds to purchase it.

Libby (2008) argues OxyContin® came along at a crucial time in pain management. To properly treat many types of chronic pain, prior to the introduction of OxyContin®, doctors had to prescribe huge amounts of pain killers which inevitably drew unwanted attention from law enforcement. Not being trained in medicine, law enforcement saw huge numbers of prescriptions and did not bother to determine if they were for legitimate medical purposes. Law enforcement automatically assumed these doctors were running “pill mills.” This occurred at a time when law enforcement was losing the so-called “war on drugs” and needed a new target (scapegoat). Doctors were often portrayed as “arrogant” or “snooty” by law enforcement and thus, appropriate targets for constant investigation and harassment. Doctors were expected to know if every patient that came into their office was actually in legitimate pain or faking symptoms. In some instances, fake patients were sent into doctor’s offices in law enforcement sting operations. This led to the loss of employment and in some cases, prison for doctors and the demonization of a very good medication which resulted in

countless people in pain not being able to be properly treated. As the reward for causing these additional tragedies, many within law enforcement received promotions and saw funding increases to their respective bureaucracies.

Similar to the claims of Meier that this "tragedy" could have been foreseen, Libby (2008) argues this "witch hunt" of doctors could have been foreseen as well. He notes there have been many periods of intolerance and persecution of doctors. The first time this occurred was from 1914-1933. In the wake of the passage of the Harrison Narcotic Act, U.S. Attorneys prosecuted more than 77,000 people for violations of the act. Between 1914 and 1938 approximately 25,000 doctors were arrested for prescribing narcotics to drug addicts. According to Libby, this push to persecute doctors was led by the temperance movement and its supporters who wanted to rid the United States of all intoxicating substances. He argues the current actions of the DEA and others to persecute doctors is just another example of history repeating itself. Libby argues the war on illegal drugs has been an abysmal failure and the DEA has shifted its mission to prescription drugs to cover up this failure. However, merely going after prescription drugs would not have been enough of a distraction to satisfy the American public. To make it an acceptable distraction the DEA and others have greatly overstated the dangers of prescription drugs and demonized many doctors both to convince the American public this is an acceptable substitute, but also a just one as well.

The term moral panic was first developed by Stanley Cohen when describing societal overreactions to the deviance of youth subcultural groups (Cohen, 2002). Drugs have often been the source of moral panics (Armstrong, 2001; Goode & Ben-Yehuda, 2009; Hawdon, 2001; Jenkins, 1994). In some instances, drug panics are tied

to drug use primarily perpetuated by certain groups of people. Opium use, during the turn of the nineteenth and twentieth centuries, was often associated with Chinese immigrants (Gahlinger, 2004; Musto, 1999). Cocaine use, in the early twentieth century, was associated with blacks in the American south (Gahlinger, 2004; Musto, 1999; Spillane, 2000). Marijuana use, in the 1930s, was associated with Mexican-Americans (Bonnie & Whitebread, 1999; Gahlinger, 2004; Musto, 1999). Many have noted that OxyContin® abuse primarily began in rural areas, particularly Appalachia (Inciardi & Goode, 2003; Passik, 2001; Tunnell, 2005; Van Zee, 2009). Not only is OxyContin® associated with rural areas, the drug has even earned the nickname "hillbilly heroin" (Tunnell, 2005).

Although earlier drug panics received coverage in newspapers and magazines, the proliferation of television news and the American media's seeming need to document the next crime problem have led to an increase in the documentation of moral panics regarding drugs. Reinarman and Levine (1989) made this observation when considering the perceived crack-cocaine epidemic of the late 1980s and Jenkins (1994) later made this observation considering the perceived "ice" epidemic regarding smokable crystal methamphetamine in 1989 and 1990. The media indicated that not only were these drugs a problem in certain parts of the country and among certain segments of the population, but abuse of these drugs would soon sweep the entire country. These researchers have argued that what the media is merely documenting is the rise and fall of the use of a drug; these occurrences are cyclic and will not become especially problematic. Many have argued that OxyContin® appears to be on a similar trajectory (Baumrucker, 2001; Inciardi & Goode, 2003; Passik, 2001; Tunnell, 2005).

Although OxyContin® has only been a part of the American drug market for fourteen years, the drug has already provided a rich narrative. OxyContin® utilizes one of several different types of semi-synthetic opiates (oxycodone) to help alleviate pain and was the second pain reliever that utilized a time release formula from Purdue Pharma. Employing a time release form of oxycodone, rather than morphine (which was the active ingredient in MS Contin®); it was supposed to produce fewer side effects in patients. Additionally, utilizing oxycodone rather than morphine was supposed to give OxyContin® a better reputation than MS Contin®, since many associate morphine as medication given to the terminally ill; thus, making many people that need the medication reluctant to take it. Although many have praised OxyContin®, it has also been demonized multitudinously. Whether OxyContin® would have earned this reputation on its own or the behavior of Purdue Pharma was the driving force is unclear. Furthermore, what role the state played in allowing what many consider a tragedy is unclear as well. The OxyContin® narrative is rich, but it is still a work in progress.

CHAPTER 5
METHODOLOGY

Research Questions

The state-corporate crime field is still a comparatively young one.[48] Kauzarlich and Matthews (2006) observed that most research in the field centers around three central concerns. First, they argue that scholars have been focused on "advancing the concept (of state-corporate crime) as a legitimate form of crime suitable for criminological analysis" (p. 239). In other words, can one properly locate this conduct within the universe of criminality and do so in a way that gives it a fixed identity capable of being studies empirically? Second, they argue that scholars in this field have been preoccupied with "exposing the massive injury that can be caused by state and corporate wrongdoing" (p. 239). Such a project of documenting harm draws on a tradition reaching all the way back to the work of Sutherland. Finally, Kauzarlich and Matthews make the case that state-corporate crime scholars have been intent on "developing an integrated theoretical framework to help explain how and why state-corporate crime (and organizational crime more generally) occurs" (p. 239).

The case of OxyContin®, the product of actions and inactions of Purdue Pharma and various regulatory agencies, represents an interesting case study in state-corporate crime and a useful lens for exploring these central issues to the field. Purdue Pharma and three of its executives pleaded guilty to mislabeling OxyContin®. As part of the plea deal, Purdue Pharma paid a sizable fine. Portions of the fine settled personal injury claims, helped fund investigations of health care fraud and contributed to prescription drug monitoring programs. There is evidence that Purdue Pharma's

[48] Although many have pointed to the work of Sutherland and others as inspiring state-corporate crime.

behavior went beyond simply mislabeling OxyContin® and actually constituted blatant false advertising, a crime that Sutherland particularly deplored. Additionally, the actions of Purdue Pharma appear to have contributed to the expansion of the black market in pharmaceuticals which not only led to higher rates of addiction and drug overdoses, but may have increased the prevalence of other crimes as well. The case study that follows is organized around a series of basic questions.

First, did the abuse liability system actually fail in the case of OxyContin®? Empirically, there can be no sustained consideration of the dimensions of the case study as a state-corporate crime unless it can be established that the harms associated with the distribution of OxyContin® could have been eliminated or minimized by a properly functioning state-corporate abuse liability assessment process. This entails asking and answering a series of very specific questions. Was there sufficient information about risks associated with OxyContin® that it should not have been approved by the FDA in the first instance? Once approved (more properly as part of the approval process) was OxyContin® properly scheduled under the Controlled Substances Act, based on what was known, or could have been known at the time? Was there adequate postmarketing surveillance that would have provided reliable and timely data on OxyContin® abuse? Finally, was there a timely and adequate response to the reports of OxyContin® diversion and abuse?

If the analysis indicates that the abuse liability system failed, then the second question is this - does this case study better fit a corporate or state-corporate framework? On the corporate side, this study will examine the drug development process undertaken by Purdue Pharma and considers the extent to which Purdue

Pharma could have anticipated abuse and diversion for abuse. Related to this question is an assessment of Purdue Pharma's marketing plan, particularly whether the marketing plan was appropriate for a Schedule II drug and resulted in over-prescription. Finally, a consideration of Purdue Pharma's role also includes their efforts to monitor the sales and actual use of OxyContin®. With respect to the state's role, this study considers whether the regulatory agencies actions to combat OxyContin® abuse and diversion were adequate, based upon the information they possessed and their regulatory authority within the drug control apparatus. Specifically, were the regulatory agencies in some way powerless because they did not possess the power or means to properly regulate or were they simply derelict in their duty to regulate?

The third and final question: does the OxyContin® case study suggest a state-corporate binary relationship or one in which third-party actors and interest groups played a significant role in producing the outcomes? The current state-corporate crime literature indicates that state-corporate crimes occur when either a regulatory agency is acting in concert with the industry they are supposed to regulate, while the corporate crime model is more likely to focus on the comparative power of the state to prevent the industry they regulate from engaging in behaviors that cause societal harm. Neither approach properly accounts for third-party roles. This study will examine the OxyContin® case to consider the possible engagement of third-parties, their motives and their influence.

Constructing a Case Study

State-corporate crime posits that economic and political interests are often intertwined.[49] Michalowski and Kramer (2006) do not believe that all occasions where economic and political interests are intertwined will result in harm. Indeed, they cite many instances where the collaboration between economic and political interests has produced beneficial results.[50] In some instances though, even when economic and political interests have noble goals, these interests will fail to properly consider means that will mitigate harm. In other instances, often motivated by greed, economic and political interests have designed structures that fail to adequately protect people from harm. At its core, state-corporate crime analysis examines documented cases of societal harm (usually regarding well documented tragedies) and examines the actions and motives of the actors who created the circumstances that led to these tragedies. When the motivations of economic and political interests are less than pure, motivated by greed, or fail to adequately safeguard people from harm, state-corporate crime occurs.

Kauzlarich and Matthews (2006) note "almost all of the empirical studies of state-corporate crime are qualitative case studies" (p. 241). Studies should seek to understand the experiences of the actors involved and the victims of those actions. According to Kauzlarich and Matthews the only way to properly study this is through qualitative interviews. Although some studies have utilized interviews conducted by the

[49] As mentioned previously, state-corporate crime borrows heavily from structural or Marxian analysis.

[50] Michalowski and Kramer (2006) specifically argue "The great modernist projects to advance industrial productivity, expand communications, develop systems of public health, and extend transportation, education, entertainment, and leisure to the masses all required collaborative efforts between the worlds of government and business…" (p. 3).

researcher, greater reliance has been placed on using existing secondary data sources such as: court or congressional testimonies, interviews conducted by journalists or "watchdog groups", or by using documents. They further note "there is nothing wrong with using these sources so long as they are interpreted judiciously" (p. 244). Interviews need to be conducted when more information is required than that provided in secondary sources, although qualitative interviews are "rife with problems" and should always be used in combination with secondary sources such as those mentioned previously.

State-corporate crime analysis has typically consisted of the gathering of secondary sources, accounts of tragedies, and/or mass harms in an attempt to determine what led to these events. Specifically, state-corporate crime researchers have attempted to ascertain how regulatory structures have been created and the rationales or circumstances that led to their construction. In reaching these conclusions, researchers have typically used secondary sources to understand and evaluate the structural construction that guided regulation schemes and the motivations that created them.

Two of the better known studies of state-corporate crime illustrate the methodologies researchers have employed to advance the theory. In analyzing the circumstances that led to the explosion of the Space Shuttle Challenger, Kramer (2006) relied on the accounts of Vaughan (1990; 1996), Perrow (1999), several historians familiar with the history of NASA, the proceedings of the Presidential Commission of 1986 that investigated the explosion, and testimony before the U.S. House hearings in 1986 that investigated the explosion. By utilizing these sources, Kramer concluded that

the actions of MortonThiokiol, Inc. (the manufacturer of the solid rocket boosters) and NASA constituted a state-corporate crime. To ascertain the circumstances that led to a fire in a chicken plant in Hamlet, North Carolina, Aulette and Michalowski (1993) relied heavily on Michalowski's experience living in North Carolina. During his time in North Carolina, several of his students were factory workers and according to him, he was able to ascertain what working conditions in factories in that state were like. Additionally, Aulette and Michalowski noted that North Carolina was a "right-to-work state" without the presence of labor unions. The researchers supplemented this personal knowledge with secondary accounts of North Carolina history to develop an understanding of North Carolina politics and their support of worker safety. Lastly, the researchers utilized testimony from testimony of Congressional hearings in 1991 that investigated the fire and newspaper articles in the *Raleigh News and Observer* that documented the tragedy.

Although he is referring to the study of state crime rather than state-corporate crime, White (2008) makes several observations that are important when justifying the use of a case study in criminological studies. Crimes that are perpetuated or endorsed by states are rarely admitted to, in most cases the opposite is true; denials are often strictly adhered to despite evidence to their contrary. Government agencies will often obscure facts and there is often little consensus within the scientific community regarding the issue(s) of concern. However, multiple incomplete sources can be put together to construct "broad trends and possibilities" (p. 44). Of specific important White notes "For critical criminology, it is essential that 'evidence' becomes part of the focus of

analytical attention – how it is constructed, how it is contested and who says what and why" (p.45).

The current study will be conducted as a case study in the spirit of the state-corporate crime tradition. Three data sources will be used: qualitative interviews with participants in the abuse liability system; data collected as part of the postmarketing surveillance system; and after-the-fact reviews of the OxyContin® case, including voluminous transcripts of seven separate congressional hearings, as well as a lengthy General Accounting Office report.

Expert Interviews

This study makes use of an electronic archive of oral history interviews constructed by historians Nancy D. Campbell and Joseph Spillane. The interviews, which were collected as part of a project supported by the Science and Society Program of the National Science Foundation, the University of Michigan Substance Abuse Research Center and the College on Problems of Drug Dependence. The archives currently consists of transcripts of oral history interviews with forty-four long time substance abuse researchers. The archive represents a range of disciplinary backgrounds and experience, including chemists, pharmacologists, neuroscientists, sociologists and geneticists. In addition, the interview subjects possess a range of institutional experiences, including work within government agencies, universities, research institutes and the pharmaceutical industry.

The interviews have a particular use for this study, which is to help construct a fuller sense of the way in which the abuse liability assessment system functioned, or was understood to function. As such, this is invaluable evidence for this case study, for

it contextualizes the actual conduct of Purdue Pharma and the state in the OxyContin® case. Of course, this is not the primary purpose of the oral history archives – these interviews are primarily to situate the personal histories of the subjects within the larger story of the development of the substance abuse research field. Consequently, not all of the interviews are relevant to the current study. For instance, interview subject Howard Becker is a widely-acclaimed sociologist who has made notable contributions to our understanding the social construction of deviance associated with drug uses, but his research has not greatly contributed to the construction of the abuse liability system regarding drugs. On the other hand, some interview subjects seem ideally placed to contribute to this analysis. Ted Cicero, to take one example, conducted a number of early scientific studies that assessed abuse liability in primates, chaired the FDA advisory committee for several years and helped to construct one of the most important postmarketing drug abuse liability assessment systems. Additionally, Cicero gives his opinion regarding the OxyContin® controversy in the course of the interview.

Obviously, interviews that are similar to that of Becker will be omitted, while interviews that are similar to Cicero's will be employed to help consider several critical issues. Of particular importance are how premarket and postmarket surveillance of drugs have developed and what government has done to encourage the creation of this knowledge. Did the system work as understood and as intended in the OxyContin® case? Were Purdue Pharma and the federal government acting within the limits of scientific and regulatory competence?

Postmarketing Surveillance

Three postmarketing surveillances programs will be used to try and construct one of the first empirical summaries of the social harms associated with OxyContin®: the Drug Abuse Warning Network (DAWN), the National Survey on Drug Use and Health (NSDUH) and Monitoring the Future. These will be supplemented by seven studies conducted by researchers published in peer-reviewed journals that employed similar methodologies.

DAWN monitors drug-related hospital emergency department visits and drug-related deaths. DAWN is operated by the Substance Abuse and Mental Health Services Administration (SAMHSA) and is an agency of the United States Department of Health and Human Services. The agency is actually required by federal legislation to collect data for DAWN. Westat, an employee-owned corporation, has a contract with DAWN to collect data from over 250 hospitals. Although DAWN data is publicly available, the FDA, the Centers for Disease Control and Prevention (CDC), the White House Office of National Drug Control Policy (ONDCP), SAMHSA, state and local government agencies, DAWN member hospitals and the pharmaceutical industry for varying purposes.[51] OxyContin®-related emergency room visits are not specifically listed by DAWN, but oxycodone-related emergency room visits are listed. The number of oxycodone related visits from 1995 to 2006[52] will be obtained and reported. These numbers will be compared to the other two types of synthetic opiates that DAWN tracks: hydrocodone and methadone.

[51] For more information about DAWN see https://dawninfo.samhsa.gov/default.asp.

[52] OxyContin was first introduced in December 1995 and 2006 is the last year that DAWN has posted data for.

NSDUH is a national survey that reports usage rates for tobacco, alcohol, illegal drug, recreational use of prescription drugs and mental health within the United States. NSDUH is authorized by federal legislation. Research Triangle Institute International first received the contract to conduct NSDUH in 1988 and the contract will continue until at least 2011. The survey is conducted annually and interviews approximately 70,000 randomly selected people. The participants are at least twelve years old.[53] OxyContin® use will be tracked and reported since 2002, the first year NSDUH added the drug to the list of drugs within the survey. Unfortunately, OxyContin® is the only prescription drug listed on the survey. The rate of reported OxyContin® use will be compared to other drugs or in the case of other prescription drugs, prescription drug categories.

Monitoring the Future is an annual study of behaviors, attitudes and values of American youth. The survey interviews approximately 50,000 eighth, tenth and twelfth grade students. Follow-up questionnaires are mailed to a sample of each graduating class for a number of years after they are initially interviewed. Monitoring the Future is funded by research grants from the National Institute on Drug Abuse and conducted by the Institute for Social Research at the University of Michigan.[54] OxyContin® use will be tracked and reported from 2002 to 2008, the years that OxyContin® has been part of the Monitoring the Future survey. OxyContin® use will be compared to other drugs for comparison purposes.

This postmarketing surveillance data will be used to attempt to identify when and if it was apparent that OxyContin® became a problem drug. The reported use of

[53] For more information about NSDUH see https://nsduhweb.rti.org/.

[54] For more information about Monitoring the Future see http://www.monitoringthefuture.org/.

OxyContin® and its active ingredient oxycodone will be tracked throughout the three data sets and will also be compared to other drugs. In addition, to the three postmarketing reporting services seven studies published in peer-reviewed journals will be added to the three reporting services data. Six of these studies are in-depth studies of coroners reports seeking to determine the number of deaths related to OxyContin® and the seventh study surveyed people admitted to 157 addiction treatment programs from 2001-2004.

Meier (2003) noted the DEA had claimed over 500 deaths were directly attributable to OxyContin® use. Shorty after the release of the report, the DEA was lambasted for making deeply flawed and misleading claims. The report had claimed all oxycodone-related deaths, obtained from solicited coroner's reports, were OxyContin® related. The DEA did not differentiate between deaths solely related to OxyContin® and deaths that OxyContin® was one of two or more drugs collectively responsible for death. Separate from the claims of the DEA, many other groups or individuals have claimed that OxyContin® use have caused addiction, crime and death on a wide scale. The only problem is that most of these reports are based upon either anecdotal evidence or data that has not been held up to scrutiny. The evaluation of the data obtained from DAWN, NSDUH, Monitoring the Future and the seven studies will attempt to answer two major questions: how much harm has OxyContin® caused and what data have been available to determine if OxyContin® use constituted a significant problem?

Congressional Hearings

The case of OxyContin® received considerable attention in both the media and by members of government. So much so that some have argued that "the problem" has

been overblown and could be considered a moral panic. Nonetheless, the United States Congress held seven hearings to discuss OxyContin® and the GAO completed a report as well. In some cases researchers have had problems receiving relevant materials, both the United States Congress and the GAO both have subpoena power that can compel people to appear and testify. With no criminal charges pending, no witness ever invoked the Fifth Amendment protection from compulsory self-incrimination. Congressional hearings are important resources to the study of state-corporate crime because they provide documentation of when certain questions were being asked and an idea of what knowledge existed at the time. They are routinely used when available. Since multiple hearings were conducted, it is also possible to track what questions were being asked at different points of time, what information was available that had not been considered or presented before and if there was any change in the tenor or the type of questions members of Congress posed to the witnesses.

The first set of hearings "OxyContin®: Its Use and Abuse" took place on August 28, 2001 before the Subcommittee on Oversight and Investigations of the Committee on Energy and Commerce of the House of Representatives.[55] The second set of hearings "Departments of Commerce, Justice, and State, the Judiciary, and Related Agencies Appropriations for 2002, Part 10, OxyContin®" took place on December 11, 2001 before

[55] Representatives James C. Greenwood of Pennsylvania and Charles F. Bass of New Hampshire presided over the hearing in Bensalem, Pennsylvania. Witnesses testifying before the committee were: Terrance W. Woodworth (Deputy Director, Office of Diversion Control, DEA), Andrew E. Demarest (Senior Deputy Attorney General, Office of Attorney General, Drug Strike Force Legal Service Section, Norristown, Pennsylvania), Christine Coulter (Lieutenant, Philadelphia Police Narcotics Intelligence Unit), Diane E. Gibbons (Bucks Country, Pennsylvania District Attorney), Michael Friedman (Executive Vice President, Chief Operating Officer, Purdue Pharma), Michael H. Levy (Director of the Pain Management Center, Fox Chase Cancer Center), Howard Udell (Executive Vice President and General Counsel, Purdue Pharma), Paul D. Goldenheim (Senior Physician, Purdue Pharma), Theresa Atwood (Registered Nurse) and Edward J. Bisch (father of a OxyContin overdose victim).

the Subcommittee of the Committee on Appropriations of the House of Representatives.[56] The third set of hearings "OxyContin®: Balancing Risks and Benefits" took place on February 12, 2002 before the Committee on Health, Education, Labor and Pensions of the United States Senate.[57] In December of 2003 the United States General Accounting Office released report GAO-04-110 "Prescription Drugs: OxyContin® Abuse and Diversion and Efforts to Address the Problem." In the methodology section of the report the GAO states that they interviewed Purdue Pharma officials and analyzed company documents and data. Selected Purdue Pharma sales representatives with high to midrange sales were interviewed. The GAO report conducted similar investigations with the DEA and the FDA. The fourth set of hearings "To do no Harm: Strategies for Preventing Prescription Drug Abuse" took place on February 9, 2004 before the Subcommittee on Criminal Justice, Drug Policy and Human Resources of the Committee on Government Reform of the House of Representatives.[58]

[56] The hearing was originally to be held on September 11, 2001. Representatives Frank R. Wolf of Virginia, Jose E. Serrano of New York, Harold Rodgers of Kentucky, Alan B. Mollohan of West Virginia and Tom Latham of Iowa presided over the hearing. Witnesses testifying before the committee were Asa Hutchinson (Administrator, DEA), Tammy McElyea (Commonwealth Attorney, Lee County, Virginia), Steven Hudson (Lieutenant, Prince William/Manassas Narcotics Task Force), Rod Maggard (former Police Chief, Hazard, Kentucky), Rick Hall (Captain, West Virginia State Police), Rolly Sullivan (Professor of Behavioral Medicine and Psychiatry and Director, Addictions Programs, West Virginia School of Medicine), Donnie Coots (father of an OxyContin addict), Paul Goldenheim (Executive Vice President for Research, Development, and Regulatory and Medical Affairs, Purdue Pharma), Mary Simmonds (First Vice President, American Cancer Society), Michael Ashburn (President, American Academy of Pain Management) and Peter Staats, Director of the Division of Pain Medicine, Johns Hopkins University).

[57] Senators Jack Reed of Rhode Island, Christopher Dodd of Connecticut, Hilary Clinton of New York, John Warner of Virginia and Susan Collins of Maine presided over the hearings. Witnesses at the hearing were: John Jenkins (Director, Office of New Drugs, Center for Drug Evaluation and Research, FDA), H. Westley Clark (Director, Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration), Richard Payne (Chief, Pain and Palliative Care Service, Department of Neurology, Memorial Sloan-Kettering Cancer Center), Art Van Zee (Lee Coalition for Health, St. Charles, VA), Nancy Green (Neighbors Against Drug Abuse), William Bess (Lieutenant, Drug Enforcement Division, Virginia State Police) and Paul Goldenheim (Vice President for Research, Purdue Pharma).

[58] The hearing took place in Winter Park Florida and Representatives Mark Souder of Indiana, John Mica of Florida, Charlie Norwood of Georgia and Ric Keller of Florida presided over the hearings. Witnesses before the hearing were: William Fernandez (Director of Central Florida High Intensity Drug Trafficking

The fifth set of hearings "OxyContin® and Beyond: Examining the Role of FDA and DEA in Regulating Prescription Painkillers" took place on September 13, 2005 before the Subcommittee on Regulatory Affairs of the Committee on Government Reform of the House of Representatives.[59] The sixth set of hearings "Prescription Drug Abuse: What is Being Done to Address this New Drug Epidemic?" took place on July 26, 2006 before the Subcommittee on Criminal Justice, Drug Policy, and Human Resources of the Committee on Government Reform of the House of Representatives.[60] The seventh set of hearings "Evaluating the Propriety and Adequacy of the OxyContin® Criminal

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Area, Office of Drug Control Policy), Robert Meyer (Director, Office of Drug Evaluation II, Center for Drug Evaluation and Research, FDA), Tom Raffanello (Special Agent in Charge, Miami Division, DEA), James McDonough (Director, Florida Office of Drug Control), Stacy Berckes (Board Member, Lake Sumter Medical Society), Jack Henningfield (Pinney Associates on behalf of Purdue Pharma), Theresa Tolle (President, Florida Pharmacy Association), Frederick Pauzar (father of an OxyContin overdose victim), Douglas Davies (Medical Director, Stewart-Marchman Center), Paul Doering (Distinguished Service Professor of Pharmacy, University of Florida), Karen Kaplan (President and CEO, Last Acts Partnership) and Chad Kollas (Medical Director, Palliative Medicine, M.S. Anderson Cancer Center Orlando).

[59] The hearing took place in Boston, Massachusetts and Representatives Candice Miller of Michigan, John Tierney of Massachusetts and Stephen Lynch of Massachusetts presided. Witnesses testifying before the committee were: Robert Meyer (Director, Office of Drug Evaluation II, Center for Drug Evaluation and Research, FDA), Joseph Rannazzisi (Deputy Chief of Enforcement Operations and Acting Deputy Assistant Administrator, Office of Diversion Control, DEA), Steven Tolman (State Senator, Massachusetts), Brian Wallace (State Representative, Massachusetts), John McGahan (Executive Director, Cushing House) and Janet Abrahm (Co-Director, Pain and Palliative Care Programs, Dana Farber Cancer Institute and Brigham and Women's Hospital and associate professor of medicine and anesthesia, Harvard Medical School).

[60] Representatives Mark Souder of Indiana, Patrick McHenry of North Carolina, Virginia Foxx of North Carolina, Elijah Cummings of Maryland, Diane Watson of California and Eleanor Norton of the District of Columbia presided over the hearing. Witnesses before the hearing were: Misty Fetko (registered nurse and mother of a DXM and Fetanyl overdose victim), Linda Surks (mother of a prescription-drug overdose victim), Barbara van Rooyan (mother of an OxyContin overdose victim), Mathea Falco (President, Drug Strategies), Stephen Johnson (Executive Director, Commercial Planning, Pain Therapeutics, Inc.), Laxmaiah Manchikanti (CEO, American Society for Interventional Pain Physicians), Steve Pasierb (President and CEO, the Partnership for a Drug-Free America), Bertha Madras (Deputy Director for Demand Reduction at the White House Office of National Drug Control Policy), Sandra Kweder (Deputy Director in the Office of New Drugs, Center for Drug Evaluation and Review at the FDA), Joseph Rannazzisi (Deputy Chief of Enforcement Operations and Acting Deputy Assistant Administrator, Office of Diversion Control, DEA) and Nora Volkow (National Institute of Drug Abuse).

Settlement" took place on July 31, 2007 before the Committee on the Judiciary of the United States Senate.[61]

Thirty members of Congress and sixty-one people testified before the committees. In addition to the testimony, many of those that testified submitted personal statements that were more than just a transcript of their testimony. A few of the submitted statements submitted were of a quality that they could potentially be submitted to a peer-reviewed journal for publication. In addition to those that appeared to testify and submitted statements, many other witnesses submitted statements, but for one reason or another did not appear to testify. Additionally, the GAO presents information from a wide variety of sources. All told, nearly every perspective of the OxyContin® story has been told. The seven hearings transcripts and GAO report account for 1400 pages of material to evaluate.

The congressional testimony and GAO report will be synopsized in the results in a similar manner to the expert interviews with two notable exceptions: these documents provide much shorter statements by the witnesses and the witnesses represent a variety of perspectives. Witnesses can be typically be classified into the following groups: politicians, Purdue Pharma representatives, victims or family members of victims harmed by OxyContin® or prescription drug use, drug regulators, law enforcement and medical professionals. From these testimonies an attempt will be made to reconstruct some sort of timeline of what happened in the OxyContin®

[61] Senators Patrick Leahy of Vermont, Benjamin Cardin of Maryland, Arlen Specter of Pennsylvania, Jeff Sessions of Alabama and Tom Coburn of Oklahoma presided over the hearing. Witnesses before the hearing were: John Brownlee (U.S. Attorney, Western District of Virginia), James Campbell (Professor of Neurosurgery, School of Medicine, Johns Hopkins University), Khanna Vikramaditya (Professor of Law, Michigan Law School), Jay McCloskey (for U.S. Attorney, McCloskey, Mina, Cunniff & Dilworth, LLC, Portland, Maine), Virginia Pagano (Police Officer, Philadelphia Police Department, Narcotics Division), Marianne Skolek (LPN, Myrtle Beach, South Carolina) and Sidney Wolfe (Director, Health Research Group of Public Citizen).

narrative. For example: when did reports of abuse begin, how widespread were these reports and how visible were they? Beyond general questions to be answered are questions specific to certain witness classifications.

Regarding politicians: how much and when were certain types of information available to them? What types of questions were members of Congress asking? What types of emotion were the members of Congress displaying? For instance, did the members of Congress seem like they were satisfied with the answers they were obtaining from witnesses? Did the members of Congress seem to be satisfied with what was transpiring, especially the actions of various actors that affected the drug regulation apparatus?

Regarding Purdue Pharma representatives: did they believe OxyContin® would become a drug of abuse and what led them to that conclusion? When did they first learn that OxyContin® was being abused, what precautions did they take to prevent this abuse and when did they implement them? Did Purdue Pharma believe their marketing campaign was appropriate? How much blame did Purdue Pharma believe they deserved regarding problems associated with OxyContin®?

Regarding victims: how did the victims obtain OxyContin® or other prescription drugs? Were these victims being portrayed as innocents with little experience with drugs, chronic users or somewhere in between?

Regarding drug regulators: did the abuse liability system fail regarding the approval of OxyContin®, the marketing of OxyContin® and/or the postmarketing surveillance of OxyContin®? What responsibility did drug regulators have in preventing OxyContin® abuse and were they given adequate authority or means to prevent this

abuse? What changes in abuse liability assessment were made as a result of OxyContin®? Did any additional changes need to be made to stop future problems regarding the regulation of drugs? Could previous problems associated with other drugs have served as a harbinger of the problems associated with OxyContin®?

Regarding law enforcement: did they see problems with prescription drugs, when did they notice these problems and how widespread were they? Did law enforcement need additional resources to combat these problems? Could previous problems associated with other drugs have served as a harbinger of the problems associated with OxyContin®?

Regarding medical professionals: what were their opinions regarding OxyContin®? Was OxyContin® a miracle drug or was the medical utility of the drug exaggerated? Did they believe that the government's response to OxyContin® and prescription drug abuse were adequate? What concerns did they have regarding the possibility or imposition of more restrictive drug controls?

The construction of a case study cannot be completely planned out. The current study attempts to ascertain if the abuse liability assessment failed in the case of OxyContin®, did Purdue Pharma engage in corporate crime and did the failure of the regulatory apparatus to either stop or mitigate the harm that OxyContin® abuse and diversion caused represent a state-corporate crime. Although many questions have been posed, not all questions relevant to this case study can be anticipated. Indeed, answers may present themselves to which questions have not yet been developed. Therefore, it is a good possibility that the analysis of the data sources will reveal additional information that has not been presented in either the literature review or the

questions posed in the methodology. Such an occurrence is typical of case studies, especially within state-corporate crime.

CHAPTER 6
RESULTS

This chapter presents an overview of the results of the OxyContin® case study. By its very nature, much of this chapter is a detailed descriptive overview of the events surrounding Purdue Pharma's development of this new drug preparation, the approval process and the postmarketing response from both the corporation and the state. The first section of this chapter, however, places the case study in the context of a general evaluation of the abuse liability assessment system. The chapter then moves on to the particular case, first examining the development and approval stage and then concluding with a consideration of postmarketing surveillance and response.

Assessing the Abuse Liability Assessment System

As Vaughan (1983), Schwartz (1991) and Lee and Ermann (1999), suggest, it is not possible to properly assess the functioning of a corporate-state regulatory system in a particular case without understanding the manner in which that system functions more generally. This section reviews the capacity and functioning of the abuse liability assessment system at the point of OxyContin®'s development and marketing.

Predictive Assessments: Animal Studies

Animal testing is a fairly standard initial step in the determination of drug safety generally, and this is also true in the case of abuse liability. The history of animal testing in abuse liability goes back to work done at the University of Michigan in the 1920s. The oral history interviews with substance abuse researchers employed in this study reveal both the promise and limitations of animal studies. Ted Cicero's[62] research

[62] Theodore J. Cicero has a PhD in Psychology from Purdue University, is a Professor of Psychiatry and the former vice chancellor for research at Washington University in St. Louis, Missouri. He served as the Drug Advisory Committee Chairman to the FDA for six years.

on the biological effects of methadone on humans was inspired by his research on animals investigating the effects of opiates on different parts of the animal's bodies. Similarly, Roland Griffiths[63] has conducted behavioral pharmacological research in both animals and humans. Specifically, he has sought to determine what effects drugs have on both animals and humans to determine the abuse liability of the substances. Griffiths suggested this work had a positive effect on regulatory decision-making. He pointed to several trips he made in the 1980s to Geneva, Switzerland, at the behest of the World Health Organization to conduct sedative hypnotic abuse liability evaluations for benzodiazepines. This research was conducted to help inform proper international controls for this class of drugs.

On the other hand, interview subjects also argued for the limitations of animal research. Regarding the determination of abuse liability of drugs, Griffiths argues "There's a lot more that can be done and refined about those analyses. I think they're still pretty crude" (p. 10). He notes animal testing is informative regarding the potential abuse liability in humans, but "there are false positives and false negatives" (p. 11). Drug discrimination is valuable, but whenever new drugs are introduced, researchers need to be cautious in making abuse liability determinations. Griffiths argues with some drugs, abuse liability cannot properly be assessed until people have access to the new substance. Specifically, he notes humans are creative and many ways in which a drug can be misused cannot be easily foreseen. Similarly, Chris-Ellyn Johanson,[64] who had

[63] Roland Griffiths is a Professor of Behavioral Biology and Neuroscience at the Johns Hopkins University School of Medicine. He has conducted behavioral pharmacology research in both animals and humans. He has consulted with NIH, FDA, WHO, the Office on Smoking and Health, DEA and forty-five different pharmaceutical companies.

[64] Chris-Ellyn Johanson is a biopsychologist at the Neurosciences Institute at Loyola University in Chicago.

previously served as branch chief of etiology at NIDA, argued informative animal research is getting more difficult to conduct. Despite her background in developing animal research experiments, she states an increasing number of false positives are occurring. According to her, differences between animals and humans are much greater than many researchers would admit and to be informative, animal studies need "serious refinement."

The limitations of animal testing are not just the inherent ones that come from the difference between animals in a laboratory setting and humans in complex social environment. Some respondents argued the limitations were also partly the result of inadequate funding opportunities from federal agencies and an overreliance on corporate-funded studies. Despite Johanson's interest in abuse liability assessment, she does not conduct original research because funding opportunities through grants are scarce, especially through NIDA. Johanson believes this is especially troubling because according to her "our procedures are primitive, and we need a lot more refinement than we have" (p. 6). Pharmaceutical companies are the only source of funding and Johnson believes that pharmaceutical companies wanted to conduct the simplest and cheapest studies they could get by with. Johnson argues pharmaceutical companies are only worried about drug approval, not about the advancement of science.

Predictive Assessments: Human Studies

As noted earlier, some have argued with certain drugs, abuse liability cannot properly be assessed until people have access to the new substance. Griffiths observed humans are creative and many ways in which a drug can be misused cannot

be easily foreseen. Thus, human subject studies would seem to be a critical element in the predictive assessments of abuse liability.

The long term history of human subjects testing for abuse liability assessment is one of loss and diminished capacity, at least according to a number of oral history interview subjects. Much of this derives from the loss of one of the formerly central tools in human subjects testing – the captive population of addict-subjects at the federal Lexington Narcotics Hospital, also home to the Addiction Research Center (ARC). Opened in the 1930s, Lexington served as the federal government's primary location for the confinement and treatment of drug addicts. Lexington's addicts also served the human subject needs of the ARD, located on the same campus.

Charles Gorodetzky[65] worked at the hospital for more than twenty years and served as both deputy director and scientific director. According to Gorodetzky, the ARC was the only place that conducted human abuse liability studies. Pharmaceutical companies that hoped to bring a new drug to market, that had a potential abuse liability, would test their drug on patients at the hospital. The ARC did not accept money for these tests, instead conducting them to protect public health. Gorodetzky stated these studies were academic in nature to obtain greater knowledge of drugs and specifically mentioned partial agonists (he specifically mentions naloxone, naltrexone and cyclazocine) were all first tested at the center. Researchers at the center designed studies and then later made the data available to pharmaceutical companies.

[65] Gorodetzky is a physician and pharmacologist who conducted clinical research in drug metabolism and kinetics at the Lexington Narcotics Hospital for more than twenty years as part of the Addiction Research Center in Lexington, Kentucky. He served as deputy director and scientific director at the center until the practice of substance abuse research on federal inmates ended and the Addiction Research Center moved its headquarters to Baltimore, Maryland in the early 1980s. Since that time, Gorodetzky has worked as an external consultant for NIDA and in industry where his research has concerned substance abuse treatment and smoking cessation.

Gorodetzky noted the center fiercely protected their independence and would not test drugs unless pharmaceutical companies had proper FDA approval for the studies. Researchers at the ARC were very careful about avoiding perceived conflicts of interest with the pharmaceutical industry. Gorodetzky recounted one instance when a colleague at the center would not allow pharmaceutical industry representatives to even purchase him a cup of coffee.

Respondents noted the ARC was not only well-funded but it was well integrated into the other elements of the state drug regulatory system. Gorodetzky noted the ARC was essentially a sister agency of the FDA, as well as the predecessor agencies to the DEA (the Federal Bureau of Narcotics and later, the Bureau of Narcotics and Dangerous Drugs). They had similar goals, but when researchers at the center sat on FDA committees they were independent scientists.

This system unraveled in the 1970s. According to Gorodetzky, the center had a problematic relationship with the newly-created NIDA when that agency emerged in 1974. NIDA viewed the researchers at the center as their representatives instead of independent researchers. Eventually, the ARC had to cease the addiction research studies at the Lexington Narcotics Hospital. To conduct their research, the center replied upon federal prisoners that volunteered to be part of the studies. Many of these prisoners would request to be sent to the hospital and signed informed consent protocols. Gorodetzky noted "You can't coerce people into research – it has to be free informed consent. Of course, we were getting informed consent from prisoners, and that's where the ethical climate was different" (p. 17). In 1977, however, a change in Federal Rules determined federal prisoners could not give free informed consent. This

determination led to a cessation of studies; together with the closing of the Lexington Narcotics Hospital at around the same time, this development ended what had been a critically important resource for the abuse liability system, one which had been built into both state and corporate decision-making.

The post-1977 testing system seems, to the experts interviewed, more conflict-ridden than the earlier system that relied on the Lexington prisoners. While Frank Vocci[66] worked at the FDA, as part of the drug evaluation process, the agency would request companies produce abuse liability assessments regarding the scheduling of drugs. Eventually, these requests were incorporated into regulations. NIDA reviews the proposed scheduling recommendations of the FDA and provides feedback. If the two agencies do not agree, an informal meeting will be held to resolve these differences. If an agreement cannot be reached, then both agencies send their recommendations to the Assistant Secretary for Health to resolve the dispute. Vocci recounted NIDA and the FDA did not always agree on the scheduling of drugs and the FDA tended to be more conservative about scheduling. He noted the FDA often had rigid informal categories of drugs and if a substance met the requirements of those categories, the agency would place it in that schedule even if the abuse liability of the new drug appeared to be less. Vocci specifically mentioned the FDA appeared to place buprenorphine into Schedule III based upon it having a withdrawal syndrome, even though the drug appeared to have a low potential for abuse. Vocci argued the FDA appeared to be getting stricter on new drug applications, but not all abuse liability issues are foreseeable. For instance,

[66] Frank Vocci is currently director of the Friends Research Institute, which receives federal, state, county and private funding to conduct studies in the fields of substance abuse, health, HIV/AIDS, mental health and criminal justice. He previously served at NIDA as the Director of the Division of Pharmacotherapies and Medical Consequences of Drug Abuse. Before his appointment at NIDA, he spent ten years at the FDA where he helped determine drug scheduling.

buprenorphine abuse has not seemed to occur in the United States, but it has in some other countries. However, the countries where buprenorphine abuse occurs have very small heroin supplies.

Predictive Assessments: Using Analogies to Learning from Past Failures

One of the ways in which the abuse liability system has attempted to predict the potential abuse liability of drugs is by considering problems (or lack thereof) with other drugs. Certainly there was no one involved in the state-corporate regulatory system at the time OxyContin was approved that was unaware of the manner in which drug abusers had manipulated legal drug preparations in the past, or unaware of the ways in which the regulatory system has approached those cases. Sidney Schnoll[67] noted the drug pentazocine (and opiate drug marketed as Talwin®) is a drug that has been abused recreationally. Particularly in the late 1970s and early 1980s, a number of recreational opiate users would crush tablets of Talwin®, combine it with the antihistamine tripelennamine, dissolve the mixture in water and then inject it intravenously. This combination of drugs is known as "T's and Blues."[68]

Schnoll recalled arriving in Chicago at the beginning of the T's and blues epidemic; most methadone patients he observed were using the combination of drugs. In 1981, the manufacturer of Talwin® met with the FDA to discuss a reformulation of the drug to make it less appealing to recreational users. In the second quarter of 1983, the reformulated product (called Talwin® NX) reached the marketplace, combining

[67] Sidney Schnoll is Vice President for Pharmaceutical Risk Management Services at Pinney Associates, a company that serves as consultants to pharmaceutical companies. He worked for Purdue Pharma from 2001 to 2005 where he developed the RADARS System.[67] He is a Clinical Professor of Internal Medicine and Psychiatry at the Medical College of Virginia and a Voluntary Professor of Behavioral Science at the University of Kentucky. He has previously served on the FDA's Drug Abuse Advisory Committee.

[68] Pentazocine by itself is known to have low abuse potential (Showalter, 1980).

pentazocine with the opiate antagonist naloxone. For many observers, the Talwin® case showed the potential utility of creating drug formulations that would deter potential drug abusers (Baum et al., 1987), as DAWN and medical examiner mentions of Talwin® dropped dramatically after 1983. It should be noted, however, that not everyone believed the Talwin® case as a good example of the power of reformulation. Schnoll observed in his interview that the T's and blues epidemic stopped before Talwin® NX came on the market. In his view, the T's and blues epidemic had only occurred because supplies of heroin had been temporally reduced.. Once those supplies returned, the use of T's and blues ended.[69]

E. Leong Way[70] recounted similar experiences, covering many substances introduced into the market and subsequently abused. Way conducted his first researched into meperidine (a narcotic analgesic, marketed as Demerol) as far back as the mid 1940s. According to Way, Demerol had been designed as an antispasmodic and was related to atropine. Therefore, it was not supposed to have abuse liability. However, reports of addiction soon began to surface with regard to Demerol, first along with the doctors and nurses for whom the drug was most readily available; later, Demerol became one of the drugs of choice for heroin addicts having trouble finding supplies of their regular drug (not unlike Talwin, later). Way noted in his interview it had taken researchers some time to properly discover the abuse liability of Demerol and he

[69] Schnoll also observed this case demonstrated why prescription drug abuse would always be higher in rural areas, since those areas were more prone to shortages of illicit drugs like heroin or to have limited distribution networks in the first instance.

[70] E. Long Way is a Professor in the Department of Pharmacology at the University of California at San Francisco. He has been a substance abuse researcher since the 1940s.

compared this experience to the manner in which heroin had also been touted decades earlier as a non-addictive analgesic.

Way also alluded, in his interview, to perhaps the best-known instance of users manipulating a drug preparation for recreational drug abuse – the case of the Benzedrine inhaler. The first reports of abuse he had encountered were of prisoners at San Quentin Prison, who would cut open Benzedrine inhalers. A piece of filter paper could be removed that contained 100 milligrams of Benzedrine carbonate sprayed on it. First marketed in the 1930s, the inhaler became popular among U.S. servicemen during World War II and among students and truckers after the war. The abuse of the Benzedrine inhaler became a classic example of users obtaining high dosage forms of a drug and finding a way to access the entire high dosage immediately (Rasmussen, 2008).

Postmarketing Surveillance

FDA approval does not end the abuse liability assessment process. Once a company begins marketing a new substance or new drug preparation, the regulatory system relies on postmarketing surveillance as the final line of abuse liability assessment. In general, interview subjects found the state of postmarketing surveillance to be fairly poor. Most was reactive, rather than proactive – meaning the state-corporate regulatory system provided for no built-in surveillance systems. For example, although Cicero found the relationship between the FDA and the pharmaceutical industry to be unhealthy and combative, he noted once a drug was finally approved, neither side really monitored approved drugs for signs of postmarket

harm. Instead, the regulatory system relied on some fairly imprecise instruments to measure harm.

Prior to the OxyContin® case, however, there were some initial efforts to construct a more proactive and robust system. Almost simultaneous with the development of OxyContin® *w*as a protracted struggle over an opiate analgesic, tramadol, which Ortho-McNeil pharmaceutical proposed to market in the United States by the trade name of Ultram®.[71] The company believed primate studies with tramadol, as well as experience with its marketing in the European pharmaceutical market for several years, suggested that the drug had a very low abuse potential. Ortho-McNeil hoped Ultram® could be sold without being scheduled under the CSA, since the scheduling of a drug typically increases a fear of addiction associated with the drug by physicians. Under the more traditional scheduling system, Ultram® would almost certainly have been scheduled, given the chemical similarities to other categories of scheduled opiates. Instead, Ortho-McNeill contacted Ted Cicero and other addiction researchers and asked them to construct an Ultram®-specific system of postmarketing surveillance. Ultimately, the FDA made the novel decision to allow an opiate to be sold unscheduled so long as Ortho-McNeil committed to tightly monitor use of the drug.[72] Cicero cited the Ultram® postmarketing surveillance program as one rationale for the FDA requiring every new drug have risk management plans and postmarketing surveillance programs.

[71] Results from these studies can be found in Chapter 2.

[72] The results of the postmarketing surveillance of Ultram were discussed in Chapter 2.

Schnoll first became involved with abuse liability assessment with Ortho McNeil and their drug tramadol. He noted the company had obtained data from Germany that suggested tramadol had a low abuse potential. To conduct postmarketing surveillance in the United States many would chose to interview people in drug treatment, however, Schnoll noted there was "a lag time of several years before people show up in treatment programs after they start using" (p. 22). As noted previously by Cicero, health care professionals were chosen to survey since they conceivably had access and knowledge of new drugs. Additional studies were conducted based upon a "key informant network" and patients using tramadol. Schnoll noted FDA postmarketing surveillance was primitive at the time and the agency often relied on AERS (Adverse Events Reporting System), but only looked at raw numbers instead of how many events occurred per use of the drug. Schnoll argued such surveillance essentially had to come from the pharmaceutical industry because he did not believe NIDA or the FDA would fund it. As to possible biases, since the study was funded by a pharmaceutical company, Schnoll stated "None of us were making our living doing this. We all had day jobs. We all felt that our reputations were more important than anything else" (p. 23). Schnoll noted the postmarketing surveillance, in lieu of scheduling, was unique to tramadol.

In general, then, the state of postmarketing surveillance prior to OxyContin®'s approval was poor, reflecting a general attitude of disinterest on the part of FDA and pharmaceutical companies. Measures of drug harms were crude and often time-lagged; meaning new drugs of abuse were not identified by the regulatory system. As before, however, these limitations were at least partly a result of an unwillingness to improve the system. As the case of tramadol shows, the concept of building in a fully-

integrated postmarketing surveillance system was available to the FDA and Purdue Pharma in the case of OxyContin®.

General Observations of the Abuse Liability Assessment System

As Hawthorne (2005) notes, one of the most common perceptions of the regulatory apparatus is how people perceive the FDA. Much like the times of Sutherland, many people believe the FDA is either subservient to or unable to regulate powerful pharmaceutical companies. Some people put very little faith in the agency. However, many of the substance abuse researchers did not depict such a one-sided relationship between pharmaceutical companies and the FDA.

When asked to describe the drug abuse liability system, Balster stated it was "pretty good." He stated "there have not been a whole lot of really serious misses" and the FDA actually had a tendency to over-regulate (p. 11). Balster argued abuse liability is a complex process, as many factors go into drug abuse and the system was doing about as well as one could be designed. He noted pharmaceutical companies will always do cost-benefit and risk analyses and the system must have some degree of predictability due to financial obligations. Balster thought it was important that regulations be based upon science and thought Congress was ill-equipped to deal with these decisions; the public interest would be better served, he believed, if lawmakers left drug scheduling to experts.

Cicero was appointed to the drugs advisory committee in 1982, but did not officially serve on the committee until 1985. According to Cicero, a previous commissioner of the FDA "got angry at the advice he was given, so he just disbanded the committee" (p. 15). Cicero was asked and accepted the position of chairman of the

reconstituted committee. When considering the relationship between the FDA and the pharmaceutical industry, he stated “what struck me was the gulf between the two” (p. 15). Cicero stated the relationship was confrontational and it seemed to risk the public health of the United States. It seemed the FDA and the pharmaceutical industry always took opposite sides of an issue. In some cases, it almost appeared the two sides took these positions out of habit rather than purpose. Most of the information the FDA and pharmaceutical industry presented was the same, but each party seemed to interpret it differently. Cicero stated the drug advisory committee was usually in the middle of the two parties and had to try to bring them to some sort of consensus. He noted the differences of opinion were typically not about science; instead the respective positions were about preserving the power of each respective side. Cicero ended his interview by stating analgesics “are vastly underutilized in this country because of fears of addiction, which may or may not be rational” (p. 20). These drugs need to be used more often by patients who suffer from actual pain. Although risk-management programs are important, how to react to problems is still being developed. Cicero believes the FDA has made several changes that improve risk management, but ultimately, the temptation to over-schedule drugs should be resisted.

In addition to pharmaceutical companies being subjected to regulatory oversight of the FDA, other government agencies have sought an interest in scheduling drugs as well. When the CSA was passed, Jerome Jaffe[73] noted the Department of Justice tried

[73] Jerome Jaffe is a Clinical Professor of Psychiatry in the Division of Alcohol and Drug Abuse at the University of Maryland School of Medicine. Jaffe became renowned while at the University of Chicago for his support and establishment of methadone clinics. He was the first chief of the Special Action Office for Drug Abuse Prevention, a position colloquially known as the nation’s “Drug Czar.” While serving in that position, Jaffe oversaw studies of American servicemen who were identified as heroin addicts in Vietnam and the establishment of the Controlled Substances Act.

vigorously to be the government agency to decide which schedule drugs should be placed in. Jaffe believed this would have resulted in bad policy. He argued the Department of Justice had a history of exaggerating the negative effects of drugs and commonly misrepresented existing data. Jaffe noted the Department of Justice did not get the authority they sought and that was important so a scheduling system could be established by considering both the medical utility and harm associated with drugs. He was sensitive concerning the under-treatment of pain, but argued that is an issue with doctors and the responsible practice of medicine, not the CSA.

Although it seems difficult to imagine how an abuse liability system could be made perfect, the current scheme is not deficient due to the lack of will on the part of the federal government to properly regulate pharmaceutical companies. As noted, the FDA will often view information provided by pharmaceutical companies with skepticism. According to some observers, the FDA tends to be too strict. However, as Hawthorne (2005) stated, certain patient advocacy group lobbyists are actually able to put more pressure on the FDA than pharmaceutical companies. Anytime a promising AIDS or cancer treatment drug is under review, patient advocacy groups will often accuse the FDA of taking too long. Instead of a loss of corporate profits, consumer groups argue the real harm is the loss of lives waiting for new treatments.

OxyContin®: Development, Approval and Marketing

Purdue Pharma traces its corporate history back to the 1890s, though the modern version of Purdue Pharma begins with the purchase of the company in 1952 by the Sackler brothers. Purdue Pharma was never one of the large pharmaceutical firms, and at the time of the Sackler brothers' purchase was best known for its topical

antiseptic (Betadine) and laxative (Senokot), niche products of the sort major pharmaceutical companies rarely involved themselves with and more in keeping with the early history of the company as an over-the-counter drug maker (an early descendant of the old patent medicine firms). In the 1960s, the company continued working at the low-tech edges of the drug business, introducing a popular herbal product for PMS symptoms (Premens). Starting in the 1970s, however, the company began more aggressively targeting areas dominated by the major pharmaceutical firms. One notable early example was the development of Trisilate as an arthritis drug. The company repackaged a combination of old drugs grandfathered into approval under the 1938 Food, Drug, and Cosmetics Act, much to the irritation of the FDA (Elia, 1978).

The company's move into pain management seems to have been part of their plans to further expand into the territory of the large pharmaceutical firms. Research began in the early 1980s for a new controlled-release form of morphine, which could be used by patients in moderate to severe pain (the treatment of cancer patients, for example, was thought to be a critical part of the market for such a product). The new preparation, called MS-Contin®, was released in 1984. The time-release formula of MS-Contin® meant the morphine was released evenly over a twelve-hour period, a huge improvement over the typical four hour dose of morphine. Long-term pain management was made much easier by the new formulation and MS-Contin® quickly captured a large portion of the oral morphine market.

Simultaneously with the release of MS-Contin®, Purdue Pharma began promotion efforts to doctors and other healthcare professionals "about appropriate use

of opioid based medicines."[74] Purdue Pharma noted this was necessary due to medical schools providing very little instruction on pain management. According to Purdue Pharma, many physicians were unaware that morphine could be administered orally when MS-Contin® was released. Although the marketing campaign conducted by Purdue Pharma for MS-Contin® focused only on physicians, it was still quite aggressive. The FDA sent six separate warning letters to Purdue Pharma for "unsubstantiated claims of superiority" of MS-Contin® on October 15, 1993, March 25, 1994, June, 7, 1994, July 7, 1994, October 3, 1994 and November 20, 1996. The FDA required Purdue Pharma to place corrective advertisements in medical journals to rectify the unsubstantiated claims.

With the success of MS-Contin®, Purdue Pharma turned its attention to developing a similar oxycodone-based preparation. Dr. Michael Levy, Director of the Pain Management Center at the Fox Chase Cancer Center observed that while MS-Contin® "has been the standard for providing good pain prevention with twice-a-day, 12-hour dosing," oxycodone had potentially greater utility in pain management with fewer side effects than morphine. He also noted there was less of a social stigma with taking oxycodone than morphine. All that was missing was the ability to deliver the appropriately large oral doses of oxycodone that pain patients would require. The introduction of OxyContin® solved these problems in the view of Levy and others in the pain management field. Levy stated "OxyContin® has been crucial for the relief of chronic pain because it has what we feel the characteristics of an ideal opioid."

[74] This exact phrase was used by Michael Friedman during Congressional testimony.

What made the development plan for OxyContin® even more significant than simply replacing MS-Contin® (although this was important; the patent on MS-Contin® was set to expire), was the decision that Purdue Pharma made to try and expand the market for the drug. The common assumption was time-release oral opiates were to be limited to categories of severe pain, often confined to cancer patients. With the development process for OxyContin®, Purdue Pharma began to explore the willingness of doctors to use this pain management tool more broadly; including new classes of patients such as arthritis and other chronic pains not related to cancer. Additionally, the company would explore if physicians would be willing to prescribe OxyContin® to patients with moderate pain that persisted for some period of time. In 1995, with the drug nearing approval, Purdue Pharma began using focus groups of primary care physicians to determine their willingness to prescribe OxyContin® for patients with non-cancer pain. The demand existed. According to these focus groups, there was a potentially larger market, if doctors could be persuaded a new product provided effective, long-lasting analgesia and a low potential for abuse. Much of the willingness to support a new time-release pain medication came from the general and growing view in the 1980s and 1990s that pain was being undertreated. The growth of the "pain management" field helped shift the basic risk-balancing formula of addiction versus analgesia which had been in place for decades.

The existing risk formula placed virtually all of the risk concern on addiction and relatively little on effective analgesia. A leading textbook on cancer from 1952 warned physicians of the "hideous spectacle" of addiction for even terminal cancer patients. It advised doctors only minimal pain relief should be provided so a patient's dying days

would not be spent as an addict (Ebert & Kerns, 2010, p. 462). Nixon drug czar Jerome Jaffe argued most doctors either accepted the risk formula, or chose to avoid the potential problems associated with prescribing controlled substances. The result, he argued, was less prescriptions of opiates than medical circumstances probably dictated. Writing in 1985, Jaffe argued "the question now is not whether the process is effective, but what are its costs" (Jaffe, 1985, p. 409).

Jaffe recounted an episode from 1964, in which his own father died after suffering weeks of excruciating pain whose severity was so great his father prayed for death so his suffering would finally end. The supervising physician, concerned about the prospect of addiction, declined to provide what Jaffe considered effective relief. As a measure of atonement, Jaffe wrote the following in a widely-read pharmacology textbook: "No patient should ever wish for death because of his physician's reluctance to use adequate amounts of effective opioids" (Jaffe, 1985, p. 411). In 1985, Jaffe wondered "if anyone ever reads these words" (p. 411).

By the 1990s, Jaffe's personal feelings were reflected in a widespread and growing movement for effective pain management. In addition to pain management becoming a rapidly growing medical specialization, the push for greater access to pain medications was propelled by the growing power of the hospice movement, which pushed for improved palliative care and a more aggressive patient's rights movement. The United States Senate held the Pain Management and Improving End-of-life Care before the Committee on Health, Education, Labor and Pensions in 1999. Implicit in this movement was a shift in the risk-balancing formula in which effective analgesia (more accurately, access to effective analgesia) would play a far more important role.

The GAO report provides the most complete picture of the efforts of Purdue Pharma to capitalize on the newly-supportive pain management environment. The report noted Purdue Pharma encouraged physicians to prescribe OxyContin® for both non-cancer and cancer pain. The company "significantly increased" the number of sales representatives retained and used "multiple promotional approaches." It was found Purdue Pharma had provided two promotional videos that according to the FDA, appear to make unsubstantiated claims and minimized the risks of OxyContin®. The first video was distributed for approximately three years without being submitted to the FDA for approval. Purdue Pharma promoted OxyContin® as a treatment for pain caused by arthritis, injuries and chronic diseases in addition to pain caused by cancer. Sales representatives focused on physicians identified as high opioid prescribers. This group of physicians included: cancer and pain specialists, primary care physicians and physicians who frequently prescribed MS-Contin®. Sales representatives were also directed to make visits to oncology nurses, pharmacists, hospices, hospitals and nursing homes.

From the time OxyContin® was introduced to the pharmaceutical market to the July 2001 labeling change which resulted in a black box warning[75], the promotional campaign of Purdue Pharma campaign had two common themes: OxyContin® should be used as the first and last medication a patient should be treated with and treating patients with OxyContin® was easier since the medication required less doses than immediate release medications. Based upon IMS Health data[76], the DEA determined

[75] This warning was later added to warn about the possibility of addiction and abuse associated with OxyContin ®.

[76] IMS Health is a private corporation that tracks pharmaceutical sales.

OxyContin® was prescribed by more physicians with diverse specializations than five other controlled release Schedule II narcotic analgesics. This caused the agency to express concern that more physicians without pain management training might be prescribing the drug.

To promote OxyContin® in 1996, Purdue Pharma employed 318 sales representatives and entered into a co-promotion agreement with Abbott Laboratories through which Abbott provided an additional 300 sales representatives to market Purdue Pharma products. In 1999, sales representatives directly employed by Purdue Pharma increased to 471. In 2000, that number increased to 562 and Purdue Pharma added a Hospital Specialty Division which employed 109 sales representatives. In 2002, Purdue Pharma employed 641 sales representatives, an additional 126 representatives in the Hospital Specialty Division and continued with the co-promotion agreement with Abbott Laboratories which resulted in a total of 1,067 sales representatives marketing Purdue Pharma products.

Sales representatives of Purdue Pharma were expected to visit thirty-five physicians a week and typically visited each physician in their sales area every three to four weeks. The company stated their compensation package was “better than industry average.” Sales bonuses were based on whether representatives met their quotas for all Purdue Pharma products. The growth of OxyContin® prescriptions resulted in increases of the quotas to reach additional bonuses. In 2001, after meeting with the U.S. Attorney for the Western District of Virginia, Purdue Pharma decided to limit sales bonuses on the basis of an increase in one physician increasing their the number of OxyContin® prescriptions written.

During the first five years OxyContin® was marketed, Purdue Pharma conducted over forty national pain management speaker training conferences at resort locations (the report specifically mentioned Boca Raton, Florida and Scottsdale, Arizona). Before this practice was discontinued, over 5,000 physicians, pharmacists and nurses were paid travel, lodging and meal costs for attending the conferences and had a speaker bureau list of 2,500 physicians during that time. During this same time period Purdue Pharma sponsored more than 20,000 pain-related educational programs through direct sponsorships or financial grants. The company also sponsored training at hospitals to comply with the Joint Commission on Accreditation of Healthcare Organizations pain standards. Purdue Pharma was one of two companies funding the educational programs and the only company allowed to distribute educational videos about pain management at the programs.

Before July 2001,[77] Purdue Pharma distributed 34,000 coupons to physicians for free trial prescriptions of OxyContin®. The coupons could only be redeemed at participating pharmacies. During 1998 and 1999, the coupons were good for a free thirty day supply of OxyContin® and from 2000 to 2001 the coupons were good for a free seven day supply of OxyContin®. The GAO noted two controlled-release morphine products manufactured by other pharmaceutical companies, Kadian® and Avinza®, were both promoted with coupon programs with the latter drug requiring a copayment. Purdue Pharma maintained several websites such as “Partners Against Pain” which had contained some information about OxyContin® and had a “Find a Doctor” feature which allowed a potential patient to find physicians who specialized in pain management.

[77] During that month Purdue Pharma and the FDA agreed to a strengthened “black box” warning for the label of OxyContin which is discussed in more detail in a later section.

Additionally, Purdue Pharma was listed as a donor on the American Pain Society website. Despite frequent claims by Purdue Pharma the company did not advertise directly to consumers, such tactics could be used to refute the company claim. Lastly, Purdue Pharma distributed many promotional items with the word OxyContin® on the items to health care practitioners including: fishing hats, stuffed plush toys, coffee mugs with heat activated messages, music compact discs, luggage tags and the pens with the conversion chart. In May of 2002, Purdue Pharma ordered all sales representatives to destroy all promotional materials that were not health-related promotional items. The following year, the company distributed OxyContin® branded goniometers, range and motion measurement devices.

One of the questions many wanted answered was when it was first known the time release capsule of OxyContin® could be crushed and bypassed. Although very few witnesses argued this was a fatal flaw that should have prevented the drug from being approved, many argued an antagonist should be added to help prevent potential recreational users of OxyContin® was crushing the drug. Steven Johnson (2006), the Executive Director of Commercial Planning for Pain Therapeutics, Inc. stated his company was developing a controlled release form of oxycodone called Remoxy which delivered the drug via a gel capsule that could not be bypassed as an alternative to OxyContin®. Johnson argued since the FDA did not require pharmaceutical companies to manufacture abuse-resistant drug formulations, many companies did not see any reason to develop them. He believed most pharmaceutical companies only cared about FDA approval and profits. During Johnson's testimony he recounted the many different

ways his company had considered a medication could be abused; something many others (such as the FDA and Purdue Pharma) did not give much thought to.

Dr. John Jenkins (2002), Director of the Office of New Drugs at the Center for Drug Evaluation and Research of the FDA stated the agency was aware at the time of approval OxyContin® could be crushed, but did not think this would be a problem since MS-Contin® or the controlled release Duramorph® were not known to be abused. The agency believed there would be less abuse of OxyContin® than other drugs due to the time release capsule. Jenkins argued there was no reason to think OxyContin® would be any different. He stated when taken as directed, OxyContin® was an effective medication and the FDA did not require the addition of antagonists to drugs. No drug was absolutely safe and there are always some adverse reactions. Indeed, Jenkins argued adding an antagonist would not curb oral abuse and would probably lead to a decrease of the efficacy of OxyContin®.

One of the limitations of the MS-Contin® analogy was that it appeared to have prevented consideration of other relevant analogies. There is no evidence, for example, the Demerol, Talwin® or Benzedrine cases were ever a part of the discussion of OxyContin®. Rick Hall (2001), a Captain in the West Virginia State Police, noted in the mid-1980s there had been a Tylox® "epidemic." He noted addicts were snorting and injecting the five milligram capsules of oxycodone after opening the capsule. Hall and others also mentioned a controlled release form of hydromorphone called Dilaudid®. These witnesses noted the drug was abused so often it had acquired the nickname "drugstore heroin." This testimony offers a compelling foreshadowing of the OxyContin

problem, but there is no evidence similar sorts of testimony was either available or presented at the drug approval stage.

OxyContin® Abuse, Diversion and Harm

One of the most controversial topics regarding OxyContin® is exactly how much harm the drug has caused. As noted previously, postmarketing surveillance within the abuse liability system (especially before OxyContin®), is woefully inadequate. Aggravating this problem is prescription drugs are supposed to be available to patients who need these medications; illegal drugs are generally forbidden. If a person is caught with cocaine or heroin, there is no legitimate reason to justify their possession of the drug. One of the main goals of the war against illegal drugs is limiting the supply of illegal drugs. Such a goal is hard with prescription drugs when there are patients who need medication. Law enforcement is left with the problem of distinguishing between the legitimate and illegitimate usage of prescription drugs. Many have noted this is a difficult and time-consuming process. The Congressional hearings are useful for tracking the development of postmarketing abuse, because the timing of OxyContin®-related harms was one of the primary factual questions at issue in those instances. Following its release into the United States market in 1996, there appear to have been some small number of cases coming to the attention of public health authorities within a year or two, but in a relatively small primarily rural geographic area (an area encompassing southwestern Virginia, eastern Kentucky and West Virginia).

William Bess (2002), a lieutenant in the Drug Enforcement Division of the Virginia State Police, stated there were thirteen reports of OxyContin® diversion in 1997. Rick Hall (2001), a captain in the West Virginia State Police, stated OxyContin® abuse

began during the summer of 1998 in West Virginia. Dr. Rolly Sullivan (2001), a Professor in the West Virginia School of Medicine, stated he first heard of OxyContin® abuse in early 1999 from a drug counselor in Charleston, West Virginia. Witnesses testified OxyContin® abuse began in southwestern Virginia and eastern Kentucky in 1999. In each of these cases, however, these were fairly localized outbreaks of OxyContin® abuse, observed by front-line law enforcement, public health and the drug treatment personnel.

Just when the problems of OxyContin® abuse reached the attention of either the company or the regulators is harder to assess for certain. The first definitive point of contact came from Jay McCloskey (2007), a U.S. Attorney in Maine, who later testified he first became aware of OxyContin® abuse in late 1999, when OxyContin® abuse became more widespread in that state (Maine was another early center of abuse). McCloskey sent a letter to Purdue Pharma in February of 2000 regarding the abuse, but did not meet with corporate executives until September of 2000, despite the executives requesting a meeting in March. McCloskey would later testify he regarded the problem as a still new and emerging issue and he did not see how Purdue Pharma could successfully intervened at that point until more was known about the extent of the problem.

By 2001, many observed OxyContin® abuse was starting to spread to urban areas and media coverage of the drug was becoming very extensive. Boston, Massachusetts and Philadelphia, Pennsylvania were both cities reporting abuse of the drug. Yet, not all areas seemed to be equally susceptible. Asa Hutchinson (2001), former Administrator of the DEA, at that time, would observe OxyContin® abuse did not

appear to be occurring at a great level in California. He surmised this was probably due to the long established and strict prescription drug monitoring program in the state which would allow fewer opportunities for diversion of prescription drugs.

By the mid-point of 2001, there was no longer any doubt OxyContin® had become a major drug abuse story in the United States, at last with regard to media coverage and political interest. At the August 2001 Congressional hearing Andrew Demarest (2001), a Senior Deputy Attorney General of Pennsylvania stated OxyContin® abuse and misuse were "exploding" in the state. In the previous two years nearly one hundred investigations had been conducted by his office. Three other witnesses testified oxycodone related deaths had increased. At the December 2001 hearing, witnesses from Kentucky, Virginia and West Virginia stated crime appeared to be on the rise due to OxyContin® abuse and diversion and many people had been affected. In subsequent hearings witnesses would state problems had occurred in Florida, Maine and Massachusetts as well. Beyond establishing what happened and when, establishing any sense of the true harm OxyContin® has caused has been difficult. Many stories are anecdotal and lack any hard data or any sense of a scope of the problem. Actual postmarketing surveillance had only a few "authoritative" data sources at that time, which are reviewed here.

DAWN Data

DAWN data were, after the anecdotal and personal accounts, the most often-cited source of information on the OxyContin® problem. DAWN, which stand for Drug Abuse Warning Network, is a public health surveillance system that reports drug-related emergency room visits and drug-related deaths reported by medical examiners and

coroners. The most immediate and obvious problem with the DAWN data throughout this period is that it was not capable of distinguishing OxyContin® from other sorts of oxycodone-based drugs (such as Percocet®), since there is really no way to definitively do so. The data does, however, show a substantial increase in the overall numbers of narcotic analgesic-related visits. From 1995 to 2002 there was 163 percent rise, from 2000 to 2002 there was a forty-five percent rise and from 2001 to 2002 there was a twenty percent rise in visits mentioning narcotic analgesics/combinations. In 2002, there were 22,397 emergency room visits attributed to oxycodone/combinations, compared to 25,197 visits for hydrocodone/combinations and 11,709 visits for methadone (SAMHSA, 2003).

In 2006, 64,888 emergency room visits were attributed to oxycodone/combinations, compared to 57,550 visits for hydrocodone/combinations and 45,130 visits for methadone. The total number of visits attributed to narcotic analgesics was 201,280. Oxycodone accounted for 32.23% of mentions for that class of drugs (SAMHSA, 2008). Thus, by 2006 oxycodone-related emergency room visits had surpassed hydrocodone visits. Yet, what seems more glaring is the large increase in mentions of methadone. Such a trend was not due to an increase in diversion at methadone clinics, but instead was due to more physicians prescribing methadone as an analgesic. This finding does not necessarily show methadone was becoming a problem drug, just a more available drug. Pharmaceutical alone visits increased 44% from 2004 to 2006. 58% of suicide attempts involved benzodiazepines or antidepressants and 45% involved CNS agents. Hydrocodone/combinations were mentioned in approximately 2,000 more suicide visits than oxycodone/combinations.

Thus, it turns out at least among persons attempting to kill themselves; there are many other drugs besides OxyContin® that should be considered problems. Oxycodone/combinations emergency room visits increased 56% from 2004 to 2006, compared to hydrocodone/combinations (44%) and morphine/combinations (46%) (SAMHSA, 2008).

The other great limitation of the DAWN data, which has been observed many times, is emergency room and medical examiner reports cannot or do not effectively link the presence of the drug to the cause of admission or death. During his expert interview, Jerome Jaffe noted in some cities (he especially noted New York), certain medical examiners critical of methadone programs would determine a death was methadone-related even if a person was hit by a truck. Most people admitted to emergency rooms have engaged in polydrug use. Several witnesses testifying before Congress argued oxycodone-related deaths had increased after OxyContin® was introduced to the pharmaceutical market and essentially argued *res ipsa loquitur*.

NSDUH Data

The National Survey on Drug Use and Health (NSDUH is an annual nationwide survey of randomly selected United States residents aged twelve or older, which has been conducted since 1988. Among the kinds of behavior the survey tracks is non-prescription drug use, defined in the survey as use of prescription drugs either "not prescribed for you" or taken "only for the experience or feeling it caused." The NSDUH did not begin asking about OxyContin® specifically until 2002 (when 0.8 percent of respondents twelve and over indicated they had "ever used" the drug). The NSDUH later added questions regarding past year and past month OxyContin® use; when these

were added to the survey in 2004, it made OxyContin® the most carefully-studied prescription drug in the NSDUH since it is the only prescription opioid inquired about by name.

Data for OxyContin® first became available in 2002, after problems with the drug seemed well underway. The lifetime prevalence of OxyContin® did rise from 0.8 in 2002 to 1.2 in 2003 and then slowly continued rising until it reached 1.9 percent in 2008 (the past year prevalence started at 0.5 percent in 2004 and has effectively stayed the same, as has the 0.1 past month prevalence. Placed in some perspective, lifetime use of OxyContin® in 2008 was 4,842 as compared to: pain relievers (34,861), tranquilizers (21,476), methamphetamine (12,598), marijuana (102,404), cocaine (36,773), LSD (23,547), and PCP (6,631) (SAMHSA, 2009).

In sum, the NSDUH survey appeared fairly late in the game, though it did, unlike DAWN, give some OxyContin-specific data. Yet, there are still severe limitations of the data. The NSDUH lumps pain relievers into one general category. It makes no attempt to distinguish among different types of pain relievers except for OxyContin®. As mentioned previously, other oxycodone-based medications, such as Percocet®, Percodan® and Tylox®, have been abused and diverted. This does not include hydromorphone-based medications, such as Dilaudid®, hydrocodone-based medications, such as Lortab® or Vicodin® and many other types of pain relievers that are being abused and diverted. Therefore, it cannot be ascertained from this data if OxyContin® was really any worse than other prescription drugs or was actually the victim of negative media attention.

Monitoring the Future Data

The Monitoring the Future survey, conducted each year since 1975 by the University of Michigan Survey Research Center and support by the National Institute on Drug Abuse, is among the longest running national surveys on drug-taking behaviors. The survey reaches nationally representative samples of about 16,000 eighth, tenth, and twelfth grade students. As with NSDUH, Monitoring the Future added questions specifically focusing on OxyContin® and Vicodin® starting with their 2002 survey. According to Monitoring the Future[78], in 2008, Vicodin® and OxyContin® usage rates had not changed significantly since peak levels were reached in previous years. From 2002 to 2008 the following percentages annual use of all students surveyed reported using OxyContin®: 2.7, 3.2, 3.3, 3.4, 3.5 and 3.4 as compared to Vicodin®: 6.0, 6.6, 5.8, 5.7, 6.3, 6.2 and 6.1. For comparison purposes, in 2008 the following percentages of annual use were reported for the following drugs: marijuana (21.5), inhalants (6.4), LSD (1.9), cocaine (2.9), amphetamines (5.8), Ritalin (2.6), methamphetamine (1.3), tranquilizers (4.3) (Johnston et al., 2009).

NSDUH and Monitoring the Future Data share some of the same liabilities. First, there is a considerable time-delay between the origins of a new drug problem as the ability of the large-scale surveys to respond. OxyContin® had clearly become a regional drug issue by 1999 and the first national surveys were not conducted until 2002 (and reported still later, when the data was finally published). Even when the national surveys began collecting data, they had limited or no ability to catch the geographic focus of drug-taking. Therefore, regional problems with specific drugs remained under-

[78] Monitoring the Future in 2008 sampled 16,300, 15,500 and 14,600 secondary school students in the eight, tenth and twelfth grades, respectively, from 386 secondary schools.

examined. Second, when the surveys responded to the OxyContin® uproar by adding the drug to their surveys, NSDUH did not add other prescription opioids for comparative purposes inquired about by name and Monitoring the Future only added Vicodin® (which turned out to be abused almost twice as often as OxyContin®). Not only is there a problem because there is almost no basis for comparison, but the study runs the risk of misidentification due to the possibility of people using other opioids (such as Percocet®, Percodan® or others) and stating the drugs they used were OxyContin®.

Although these critiques of the postmarketing surveillance may seem telling, the GAO report concerning OxyContin® noted many of the deficiencies of the postmarketing data. "The databases the DEA[79] uses to track the abuse and diversion of controlled substances all have limitations that prevent an assessment of the relationship between the availability of OxyContin® and areas where the drug is being abused or diverted. Specifically, these databases, which generally do not provide information on specific brand-name drugs such as OxyContin®, are based on data gathered from limited sources in specific geographic areas and have a significant time lag. As a result, they do not provide reliable, complete, or timely information that could be used to identify abuse and diversion of a specific drug" (GAO, 2003, p. 32). So not only did OxyContin® fail to stand out or present itself as a problem in the postmarket surveillance data, the quality and timeliness of the data has been questioned as well.

Other Postmarketing Studies

[79] As mentioned previously, in addition to tracking DAWN, NSDUH and Monitoring the Future, the DEA purchases data from IMS Health and receives data for ARCOS (Automation of Reports and Consolidated Orders System) which like the IMS Health data, only tracks sales of prescription drugs.

In the immediate period following the extensive reporting of problems with OxyContin®, a number of research studies attempted to supplement the limited data available in the standard data collections. Several researchers conducted studies in particular to better understand how many drug-related deaths could be attributed to oxycodone, OxyContin®, other drugs or polydrug use. It is important to note Purdue Pharma funded several of these studies, but these findings support what many witnesses stated before Congress; most drug-related deaths are attributable to polydrug use, not any one single drug.

Using what they call "A DAWN-based Classification Scheme"[80] Cone et al. (2003) found only thirty of 919 drug abuse deaths had oxycodone as the single reported chemical entity and only in twelve of those thirty was OxyContin® identified as the source of oxycodone.[81] It was further noted 96.7% of deaths were caused by polydrug use. This point is important considering in a follow-up study Cone et al. (2004) found oxycodone is more toxic when used in combination with other drugs.[82] Carson (2007) had similar findings when analyzing twenty-four cases of multiple drug intoxication. In a study examining 172 deaths involving oxycodone in Palm Beach County, Florida Wolf, Lavezzi, Sullivan and Flannagan (2005) found eighteen of those deaths were attributed to oxycodone toxicity (in combination with other drugs) and eight deaths were attributable to oxycodone alone. In a study of 2024 deaths reporting analgesic- and cough suppressant-opioids in England and Wales it was found t in 93% of cases the

[80] The researchers created a postmortem database using 1243 solicited cases from medical examiners and coroners offices in twenty-three states from August 27, 1999 to January 17, 2002 (Cone et al., 2003).

[81] Purdue Pharma funded Cone et al. (2003).

[82] Purdue Pharma funded Cone et al. (2004).

death occurred from polydrug use (Schifano et al., 2006). In Hennepin County, Minnesota it was found of sixty-seven oxycodone positive deaths from 2000 to 2005 thirty of the cases were drug overdoses. Of those thirty, seven were identified as deaths from oxycodone alone (Thompson, Vanderwerf, Seningen, Carr, Kloss & Apple, 2008). Among 21,460 deaths in Cuyahoga County, Ohio fifty-five deaths tested positive for methadone, 190 deaths tested positive for oxycodone and 200 deaths tested positive for hydrocodone. In 135 of the 190 cases involving oxycodone the presence of the drug was an incidental finding. Of the fifty-deaths attributed to oxycodone, fifteen were due to oxycodone intoxication (Baker & Jenkins, 2008).

Rather than conducting a follow-up of drug-related deaths, one study investigated drug use among admissions to drug rehabilitation. During his Congressional testimony, Dr. Rolly Sullivan (2001) noted at one time every person in his drug rehabilitation clinic in Morgantown, West Virginia was addicted to OxyContin®. In a more comprehensive study of 27,816 subjects admitted to 157 addiction treatment programs in the United States from 2001-2004 it was found approximately 5% of the subjects had used OxyContin® and 78% of those subjects did not have a prescription for the drug (Carise, Dugosh, McLellan, Camilleri, Woody & Lynch, 2007).

These studies illustrate one of the major problems in identifying potential drug epidemics. Drugs that utilize the same basic compounds as other drugs, such as oxycodone, cannot be specifically identified. The vast majority of deaths in these studies were due to polydrug use. Additionally, although one witness before Congress stated OxyContin® abusers or addicts represented a huge portion of those seeking treatment; that was not the experience of most drug rehabilitation centers.

Postmarketing Response: A Chronological Narrative

In addition to determining what information was available (regarding the dangers associated with OxyContin®) is discovering what actions Purdue Pharma and various regulators took to prevent the abuse and diversion of OxyContin® after the drug was given FDA approval, especially after reports of abuse and diversion became known (or should have been known). Laufer (1994) noted the liability of a corporation is often determined both by how the company prevented and dealt with corporate harms (proactive and reactive fault) and/or examining either the corporate ethos or the corporate policies which may have encouraged or caused corporate harms. State-corporate crime researchers have examined the actions and policies of state regulators that have either encouraged or allowed corporations to engage in actions that have led to the victimization of citizens. Some studies have also stated state-corporate crimes occur through acts of omissions on the part of the state; arguing a failure to regulate is a crime by the state. Examining these actions will be crucial in determining if the circumstances indicate this was a case of corporate crime and/or state-corporate crime.

The “response” phase effectively began in 2001, when U.S. Attorney McCloskey contacted Purdue Pharma and the DEA about problems with OxyContin® in Maine. Prior to 2001, there was not an effective response by the regulatory system or by Purdue Pharma, primarily because the existing sources of postmarketing data had not yet revealed the extent of any misuse of the drug. The defect in the abuse liability system, at that point, was not specific to the actors in the case, but a more general defect of a system that was designed in such a way that it could respond only slowly to

emerging drug problems and then only with blunt or potentially misleading sources of data.

By 2001, the appearance of a problem could no longer be denied, even if the scope and nature of the problem remained somewhat unclear. In addition to McCloskey's contact, the first Congressional hearing was scheduled for August of 2001, with a second held in December of the same year. The response of Purdue Pharma at these first two hearings gives a good sense of what the company's approach to the OxyContin® issue was at that point. Purdue Pharma seemed to have had genuine skepticism about the magnitude of the problem; rather than denial of an obvious reality, the company appeared to have genuine doubts that the OxyContin® problem was of a serious magnitude. According to Purdue Pharma representatives at the 2001 hearings, reports of harm associated with OxyContin were overblown

In response and based on their own doubts, Purdue Pharma paid for the establishment (in 2002) of the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS) program to help assess and monitor OxyContin® abuse; a surveillance program with which interview participant Ted Cicero would become closely associated.[83] Cicero's interview suggests Purdue Pharma helped construct the RADARS system to validate the company belief the media stories regarding the extent of OxyContin® abuse were being exaggerated; however, Cicero argues abuses associated with OxyContin® were not exaggerated. He notes Purdue Pharma "really

[83] The RADARS System External Advisory Board included: Edgar Adams of Harris Interactive, John Burke of the National Association of Drug Diversion Investigators, Ted Cicero of Washington University, Richard Dart of the Rocky Mountain Poison and Drug Center and the University of Colorado, Dana Droz of the National Association of State Controlled Substance Authorities, Anne Geller of Columbia University, James Inciardi of the University of Delaware, Herbert Kleber of Columbia University, Alvaro Munoz of Johns Hopkins University, Edward Senay of the University of Chicago and George Woody of the University of Pennsylvania.

erred in the way they marketed the drug" (p. 19). According to Cicero, Purdue Pharma was still maintaining their original argument the drug was "impervious to abuse" due to the time-release capsule (which they argued could not be bypassed) and slow-acting drugs are rarely abused. He noted addicts, who are typically clever, realized almost immediately the time-release capsule could be bypassed and blames OxyContin® abuse as "the trigger for the initiation of prescription opioid analgesic abuse which is now reaching epidemic proportions in this country" (p. 19).

Another interview subject, Sidney Schnoll, was approached by Purdue Pharma in 2001. Purdue Pharma hired him, based upon his experience in helping establish the programs to monitor tramadol use, to establish the RADARS system. Like Cicero, Schnoll believes the company genuinely did not have a true sense of the OxyContin® problem. Based on the negative media exposure, Schnoll recalled, the company wanted to determine if the reports were accurate and did not have the means to collect usable data without constructing an entirely new surveillance system. Schnoll argued the traditional postmarketing reporting services were geared towards illegal drugs. When questions asked about prescription drugs were asked, whole groups of prescription drugs were often lumped together or only a few drugs would be identified, which might lead to the inflated occurrences of those drugs.

Schnoll noted once the RADARS system was established, it was found OxyContin® abuse was highly regionalized, much like the abuse of other drugs. In addition to the reporting system, a group of field researchers that followed up reported cases of OxyContin® abuse found in many cases, reports of abuse were actually misidentified and other drugs were the culprit. It is worth noting Schnoll found the

RADARS data to be unexceptionable; the media coverage, in his view was still grossly distorting the true nature of the problem, as it had with amphetamine use in the 1960s and 1970s, Quaaludes and benzodiazepines such as Xanax and Halcyon. According to Schnoll, attention is given to whatever "the drug du jour" is at that moment in time (p. 26). He argued this is a continuing failure of policy and the root causes of drug abuse are never addressed. According to him drug abuse is a symptom of larger and more complex issues.

This position, it should be noted, had the support of many in the drug addiction research community. At a 2002 Congressional hearing, Dr. Westley H. Clark, Director of the Center for Substance Abuse Treatment at SAMHSA, began his testimony by stating the current problem with OxyContin® is "merely the newest part of a prescription opioid diversion and abuse problem that has been rising since the mid-1980s." He noted the rate of new prescription opioid abuse and abusers and been rising steadily before OxyContin® was introduced to the pharmaceutical market. Clark specifically mentioned, according to DAWN data, hydrocodone was mentioned twice as often as OxyContin®. He continued "we are dealing with a larger global issue of prescription drug abuse and it is important that we keep this in mind as we develop strategies of prevention." Clark stated prescription opioid abuse has occurred in rural areas for some time. Clark noted the proposed budget for FY 2003 had an $127 million increase for drug treatment. He noted this was important due to an estimate that over one million Americans were addicted to opioids and only 200,000 were officially in treatment. Clark noted treatment efforts were expanding in many states as well and the potential approval of Buprenorphine would help treat opioid addiction and dependence. He noted

most people with pain who take OxyContin® do not become addicted. Pain patients who become addicted to medications usually have a previous history of addiction or substance abuse.

The second position of Purdue Pharma at this point was to assert the company could not have anticipated whatever cases of abuse had taken place and the existing regulatory apparatus was sufficient to handle whatever issues might arise. Company representatives acknowledged Purdue Pharma had been was aware the controlled release mechanism could be bypassed, but it was largely unforeseen this would occur (based upon the company experience with MS-Contin, but as many noted, MS-Contin could not be crushed in a similar manner). Furthermore, Purdue Pharma should not be held responsible for the actions of "drug addicts" who were misusing a valuable medication in a manner in which the instructions of the drug clearly stated not to. Additionally, since OxyContin® was a Schedule II drug, Purdue Pharma argued physicians should have known the drug was dangerous. However, Purdue Pharma also noted many physicians are poorly trained in pain management and might not have a good background in prescribing the appropriate amount of medication to appropriate patients.

Purdue Pharma continually stated OxyContin® abuse and diversion were just one part of a much larger societal problem with prescription drug abuse. The company stated the only solution to this problem was more education and the implementation of prescription monitoring programs. It was repeatedly noted many people, especially teenagers and younger drug abusers, did not understand prescription drugs could be as dangerous as illegal drugs. Purdue Pharma noted the company only sold OxyContin®

(and other drugs produced by the company) to wholesalers and afterwards the company was not able to monitor who the drug was sold to. Therefore, the company could not refrain from selling OxyContin® to places suspected of diverting the drug. Additionally, Purdue Pharma argued it was the job of law enforcement to investigate abuse and diversion and the company lacked the investigative resources via the criminal justice system to conduct these types of investigations. The company further stated the only action available to the company was to refrain from sending sales representatives to places where diversion was suspected.

The third position of Purdue Pharma at this point was to strongly reassert the risk-balancing formula that assigned significant weight to the problem of the undertreatment of pain. Particularly at the 2001 and 2002 Congressional hearings, company representatives expressed a need for balance and caution. The company continually cited statistics stating how great a problem untreated pain was in the United States. Purdue Pharma continually noted the millions of dollars in lost productivity from people having to take sick leave from work and the pain they suffered due to a lack of access to prescription medications and inadequate pain treatment. The company argued whatever actions were taken in response to OxyContin®, these actions should not come at the expense of people who were suffering. Purdue Pharma noted in previous years, society was more draconian and did not allow patients appropriate access to pain medications. The company stated it was important not to return to that regulatory climate.[84]

[84] Dr. Michael Levy (2001a), Dr. Mary Simmonds (2001), Dr. Michael Ashburn (2001), Dr. Richard Payne (2002), Dr. Stacy Berckes (2004), Dr. Karen Kaplan (2004), Dr. Chad Kollas (2004), Dr. Janet Abrahm (2005) and Dr. James Campbell (2007) all stated pain was undertreated, but improvement had been

In support of the position of Purdue Pharma, the company enjoyed the testimony at the early Congressional hearings of its supporters in the pain management field, including statements from the American Pharmaceutical Association, the American Society of Pain Management Nurses and the American Academy of Family Physicians, among others. Dr. Michael Levy (2001a), Director of the Pain Management Center at the Fox Chase Center, noted his pain center treated more than 500 new patients a year. He argued "We are in the midst of two epidemics, the epidemic of unrelieved chronic pain, and the epidemic of OxyContin® abuse." He argued OxyContin® is one of the best painkillers available within the last decade and it must be readily available to treat pain. Levy stated "OxyContin® has been crucial for the relief of chronic pain because it has what we feel the characteristics of an ideal opioid." It has both a short half-life and a long duration. When taken appropriately, its formulation allows it to treat pain quicker than MS-Contin®. Levy noted that OxyContin® has been utilized by orthopedic surgeons and rheumatologists who would not consider using morphine.

Dr. Mary Simmonds (2001), the First Vice President of the American Cancer Society, Dr. Michael Asburn (2001), President of the American Academy of Pain Management and Dr. Peter Staats (2001), Director of the Division of Pain Medicine at Johns Hopkins University all gave similar testimony requesting Congress show restraint and not penalize patients who need pain medications. According to Simmonds "the hype on OxyContin® today will be repeated tomorrow with another drug, it is really the same issue and, as we have heard today, it has happened in the past already. Therefore, to focus simply on a particular opioid today is at best, I suggest, a waste of

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made and it was important not to return to a previous regulatory climate when pain medications were not largely available to pain patients.

time, and at worst might put up yet another barrier to make it even more difficult to provide pain relief to those who need it." Ashburn stated "only a qualified physician, together with his or her patient in the context of a doctor/patient relationship, has the information necessary to decide what approaches, structure, and therapeutic goals are appropriate for the management of pain in a particular situation." Staats stated "the opioid class of medication provides the most effective treatment for moderate to severe pain and could not be abandoned without grave consequences for countless individuals and for society as a whole. Instead of legitimate access to opioids therefore, we must seek strategies that will eliminate this diversion we have talked about today."

Dr. Richard Payne (2002), Chief of Pain and Palliative Care Service in the Department of Neurology at Memorial Sloan-Kettering Cancer Center made an appeal for balance in drug policy. He stated it was important not to restrict controlled substances so they were unavailable for patients suffering from pain. Payne stated opioid analgesics (he mentioned morphine, oxycodone, fentanyl and methadone) are the most effective treatment for moderate to severe pain and in some cases, the only treatment that worked. He insisted a variety of medications are needed to select the best drug for each patient. According to his experience, up to fifteen to twenty percent of patients need a drug other than morphine, due to negative side effects some patients suffer. Eighty percent of Payne's patients required at least one switch in medications, forty-four percent required two or more switches and twenty percent required three or more switches. Payne stated "OxyContin®, a controlled release formulation of oxycodone, is as effective as any other opioid for the treatment of pain." He also noted OxyContin® had similar side effects and abuse liability to other opioids. According to

Payne “The well publicized cases of OxyContin® abuse are, in my opinion, related to the fact that it is so much more widely prescribed…There is little data that oxycodone per se has any inherently increased abuse liability compared to morphine or other opioids.” Payne stated the reason OxyContin® is so widely prescribed is the drug is an effective alternative for patients that will not tolerate other opioids and generally it is much easier to adjust the dose of OxyContin® to the needs of individual patients. Additionally, the high bioavailability, short half-life, long duration of effect and predictable pharmacokinetics all make OxyContin® a popular medication, “much more so than any marketing details by the pharmaceutical industry.”

Tracking the *state* response is somewhat more complicated than tracking the response of Purdue Pharma. To begin with, the “state” in this instance is a more complicated entity than the traditional state-corporate crime paradigm tends to suggest. Drug policy is not established or regulated by any one agency or regulatory body. Here, the reaction was divided in three ways: the FDA, the DEA and Congress (though one could argue that state and local governments were also important actors in this case). Thus, federalism can complicate the process and often prevents the federal government from exploring all avenues of regulation because certain duties are reserved for individual states (such as the regulation of the practice of medicine).

The FDA responses seemed fairly consistent with that of Purdue Pharma, reflecting the shared assumptions between the two that had gone into the approval process. Dr. John Jenkins (2002), Director of the Office of New Drugs at the Center for Drug Evaluation and Research at the FDA, noted the agency had worked closely with Purdue Pharma to strengthen the warning to patients and consumers and that the FDA

had “determined that the benefits of OxyContin outweighed its risk when used to treat moderate to severe pain.” In May of 2000, the FDA sent a warning letter to Purdue Pharma concerning an advertisement in a medical journal the agency believed was “inappropriate.” Advertisements must be submitted to the FDA at the time of labeling and publication. Advertisements do not require prior approval. The agency reviews advertisements and promotional materials post hoc. If the FDA does not approve of an advertisement, the agency will either prohibit the materials from future appearances or require an additional advertisement that provides corrections of inaccuracies or misstatements. If Purdue Pharma had chosen to, the company was not prohibited from advertising directly to consumers. The advertisement the FDA believed was false and misleading implied OxyContin® had been studied in all forms of arthritis and failed to disclose the associated risks to that class of patients. Jenkins noted Purdue Pharma agreed to no longer use the advertisement and the agency considered the matter resolved.

In conjunction with the FDA, Purdue Pharma changed the warning label and added a black box warning to packages of OxyContin® on July 18, 2001. This label change added warnings of the potential of addiction associated with OxyContin® use. In addition to the new “black box” warning, Purdue Pharma and the FDA developed, a patient sheet was added warning of the dangers associated with OxyContin® and to inform patients how to properly take the medication. The FDA developed a patient-information sheet on its website with the same information.

In July of 2001, Purdue Pharma created a “hot line” for physicians to report sales representatives who did not responsibly promote OxyContin®. Purdue Pharma noted it

had distributed tamper-resistant prescription pads to physicians. By that time over 500,000 brochures had been distributed to physicians and pharmacists designed to help prevent doctor-shopping and other forms of diversion. After a robbery at a Mexico City distributor of OxyContin®, Purdue Pharma no longer shipped 40 mg strength or higher OxyContin® to Mexico and restricted which pharmacies could sell 20 mg and 10 mg strength of OxyContin®. Purdue Pharma had also spent "tens of millions of dollars" to research and develop new medications resistant to abuse. It was noted in 1996, the company had attempted to combine hydrocodone with naloxone, but it did not curb oral abuse and compromised the analgesic properties of the drug.

Throughout this period, FDA participated in an ongoing series of meetings with Purdue Pharma and other federal agencies to share information and develop new strategies to prevent abuse and diversion of prescription drugs. An FDA advisory committee meeting was held on January 30-31, 2002 to discuss the medical use of opioid analgesics. The meeting urged a balanced effort be taken to prevent abuse and did not want to reverse the recent trend to make opioids more available to patients in pain.

The DEA and Congress, on the other hand, broke from the Purdue Pharma-FDA position relatively early into the case, projecting a tougher stance and reworking the risk-balancing formula away from pain management and toward drug abuse control. Still, even this shift took some time. Representative James Greenwood (2001) (R – Pennsylvania) opened the first Congressional hearing restating the Purdue Pharma-FDA risk-balancing formula – "for some OxyContin is the angel of mercy; for others, it is the angel of death" – both the palliative and harmful effects of OxyContin®. The

December hearings opened with a similar restatement of the risk-balancing formula and an assurance to legitimate users that Congress was not trying to take away their pain medicine. At that point, the only federal agency providing testimony was the DEA and the FDA was only available for questioning, but did not present direct testimony. At this time, any anger or frustration by members of Congress was directed at Purdue Pharma.

Likewise, the initial response of the DEA was to work within the Purdue Pharma-FDA framework that had been established. In May of 2001, the agency worked with the FDA and Purdue Pharma to help develop a "comprehensive action plan" which consisted of specifically targeting key point of diversion such as "unscrupulous or unethical" medical professionals, forged and fraudulent prescriptions, pharmacy theft and doctor-shopping. Tom Raffanello (2002), a special agent in the Miami Division of the DEA, stated this was the first time the agency had taken such an action to combat the abuse of a single prescription drug. He did note, however, "the initiative is not intended to impact the availability of OxyContin for legitimate medical use." The agency claimed it lacked the authority to define what the legitimate prescribing of medicine was and instead worked with the FDA and Purdue Pharma on a program to provide information to the medical community concerning the "proper use of OxyContin®." In Congressional testimony, DEA representatives emphasized the need to collect data and to take a balanced approach toward the twin issues of pain management and drug abuse.

In 2001, the DEA collaborated with Purdue Pharma on the "100 counties" program, in which Purdue Pharma had identified the 100 counties within the United States where OxyContin® abuse and diversion appeared to be the biggest problem.

The 160 sales representatives in those counties were given intensive training, part of which the DEA participated in, to be able to better educate physicians about OxyContin® abuse and diversion. Around the same time, Purdue Pharma and begun providing placebo pills to law enforcement engaging in undercover operations. When Purdue Pharma discovered illegal online advertisements for OxyContin® pills, these were submitted to the DEA.

The February, 2002 Congressional hearing begins to show a shifting response on the part of both Congress and the DEA, toward a more open criticism not only of Purdue Pharma (which had been roundly criticized for over-promotion even in the 2001 hearings), but also to the abuse liability assessment system itself. Senators Jack Reed (2002) (D – Rhode Island) and Hillary Clinton (2002) (D – New York) offered opening statements that provided a near-perfect restatement of the Purdue Pharma-FDA risk-balancing formula, observing the significance for Congress that many people suffer from inadequately treated pain, as well as considering the crimes associated with all forms of prescription drug abuse and diversion (not just OxyContin®).[85] In contrast, Senator Susan Collins (2002) (R – Maine) concluded OxyContin® should not be dismissed as just the latest drug to be abused. Such an approach would "not fully convey the destruction of human lives caused by the abuse of OxyContin®. When talking to people

[85] Senator Christopher Dodd (2002) took a slightly different tack during his testimony when he noted "I am glad that we will also have a chance to hear from Purdue Pharma, the manufacturer of OxyContin®, which is based in my home state of Connecticut." He noted Purdue Pharma had taken many steps to curb OxyContin® diversion and abuse and stated "Purdue is clearly willing to participate in an effort to curtail the diversion and misuse of their product and I urge them to continue to do so." Dodd noted the General Accounting Office would be examining the advertising practices of Purdue Pharma and he would request the study be extended to "the entire class of medicines subject to abuse and diversion." He noted, in January of 2002, a Federal judge in Kentucky a federal judge ruled plaintiffs in a lawsuit had failed to establish a link between the marketing practices of Purdue Pharma and diversion and/or abuse. Throughout the hearing he would constantly defend the company.

on the front lines in Maine I have heard stories of lost jobs, broken families and young people who naively thought that a legal drug available at a local pharmacy could not possibly do them any real harm." She argued serious questions had been raised about the marketing of OxyContin® and stated "this issue prompts still further questions about whether additional Federal and State regulation and monitoring is needed."

Interestingly, the DEA's harder line seemed to receive a push from a few people in the medical and addiction treatment fields, who tended to see Purdue Pharma as a far more manipulative actor in the case. At a 2002 Congressional hearing, Dr. Art Van Zee (2002) of the Lee Coalition for Health in St. Charles, Virginia, stated "in the 25 years I have practiced as a general internist in St. Charles, which is a small Appalachian coal mining town, there has never been anything to compare to the epidemic of drug abuse and addiction that we have seen in the last 3 years with OxyContin." He disagreed this was just another case of drug addicts choosing a new drug to abuse and stated most of the drug abuse has been perpetuated by young people that have quickly become addicted to OxyContin®. Van Zee stated many physicians had overprescribed or misprescribed OxyContin®, the problems with OxyContin® were an example of prescription drug abuse in society and "the promotion and marketing of OxyContin by Purdue Pharma has played a major role in this problem."

Dr. David Egilman (2004), Clinical Associate Professor of Community Medicine at Brown University stated Purdue Pharma had implemented a marketing strategy to undermine patient and physicians appropriate reservations of abuse, diversion, addiction and death by overdose of OxyContin®. He stated the company implemented a labeling strategy to downplay addiction risk in the patient package inserts and in

materials prepared for distribution for patients given to healthcare providers and patients. Egilman stated Purdue Pharma misrepresented the dosing schedule of OxyContin® and the medication did not work for twelve hours. He also stated patients can and do become addicted from taking drugs that were prescribed by physicians. Egilman argued Purdue Pharma essentially created the demand for OxyContin® by continually downplaying the fears many physicians had about prescribing pain patients. Purdue Pharma did not initially warn patients about the potential for addiction associated with OxyContin® even though the company did with the drug MS-Contin®; a drug that has shown considerably less abuse potential. He stated this was done based upon the theory delayed absorption drugs are less prone to addiction, a claim he states is unsupported by scientific studies. Egilman additionally noted clinical trials would not have shown a potential for addiction based upon short term studies and these claims should have not been made until studies could have been conducted to properly assess these claims. According to Egilman, Purdue Pharma believed a twelve-hour pain relief drug would be important for marketing purposes. He stated OxyContin® is only shown to be effective for eight to ten hours and patients often needed another dose or supplemental medication before a twelve hour period expired. Egilman stated most of the information he was relying on was obtained through the discovery process in lawsuits concerning lawsuits and was not publicly available.

Dr. Rolly Sullivan (2001), a Professor of Behavioral Medicine and Psychiatry and Director of the Addictions Programs at the West Virginia School of Medicine, first heard of OxyContin® abuse in early 1999 from a drug counselor in Charleston. He noticed an increasing number of patients in his rehabilitation clinic that peaked in August of 2000.

On one day, all ten patients at the center were OxyContin® addicts. Since that time, the number of patients trailed off to about half. Sullivan stated OxyContin® seemed to be just the newest drug addicts were using and noted the area had never had a large supply of heroin which may have led to increasing usage rates of OxyContin®. John McGahan (2005), Executive Director of the Gavin Foundation, stated in the late 1980s and early 1990s people entering substance abuse rehabilitation typically had shifted from alcohol abusers to cocaine abusers. He stated most heroin users had tried OxyContin® first, but switched due to the cost of the two respective drugs.

Acknowledging the defect in OxyContin®, Purdue Pharma noted they had begun efforts to reformulate the medication so that the time-release mechanism could not be bypassed. At the August 2001 hearing, Michael Friedman stated (2001) the company has spent “tens of millions of dollars” to research and develop new medications resistant to abuse. At the December 2001 hearing, Paul Goldenheim (2001) noted the company had spent fifty million dollars in 2001 to research and develop abuse resistant pain relievers. At the February 2002 hearing, Paul Goldenheim (2002) noted the company had spent one hundred million dollars to research and develop abuse resistant medications. Goldenheim noted the process was difficult.

The issue of “reformulation” that emerged in these early hearings would become increasingly pressing as time went on. Members of Congress, in particular, seemed confused why reformulation did not happen immediately after it was clear addicts were manipulating the defect in the time-release formulation and the members became frustrated the FDA and DEA were not doing more to pressure Purdue Pharma to complete what many members seemed to think should be a simple process. Meyer

(2005) told Congress reformulation of OxyContin® represented a significant scientific challenge and the FDA could not simply order Purdue Pharma to prepare a reformulation of the drug. Another member of Congress expressed frustration with both the DEA and FDA for failing (in his view) to properly explain the steps the agencies were taking to encourage or promote the reformulation of OxyContin®. The DEA did not have a clear answer to the question which provoked an extended critical commentary on the failure of pharmaceutical companies to manufacture drugs that were abuse resistant and the limited role of state agencies in insisting on abuse-resistance was part of the criteria for the approval of an NDA.

Interestingly, the inability or unwillingness of Purdue Pharma to reformulate OxyContin® provided a competitor a Congressional platform to advertise their efforts to do precisely that. Stephen Johnson (2006), Executive Director of Commercial Planning at Pain Therapeutics, Inc., a biopharmaceutical company specializing in the research and development of safer drugs used for pain management, was invited to share information about a new drug product called Remoxy®. Remoxy® is a form of oxycodone in a highly viscous fluid formulated to resist tampering or accidental misuse. Johnson believed such a formulation was useful for the development of other drugs. His company was also developing a drug called Oxytrex, which combines oxycodone with an ultra-low dose of an opioid antagonist. Johnson had four recommendations to the committee: (1) applications to market prescription drugs specifically formulated to deter abuse or misuse should be eligible for priority review, (2) the FDA should allow labeling for drugs specifically designed to be abuse resistant, (3) risk management plans should take into account if a drug has been designed to be abuse resistant, (4)

Medicare and Medicaid should recognize the benefits of drugs designed to be abuse resistant.[86]

Along the same lines, Representative Stephen Lynch (2005) (D – Massachusetts) at a 2005 hearing put the issue bluntly: "we are here to examine the recently amended and accelerated FDA drug approval process that has somehow allowed a series of drugs to come onto the market." Lynch then tied the OxyContin® case to a series of highly publicized drug-related problems that had recently emerged, including Vioxx, the Cox II inhibitor, ephedra and Palladone, all of which had been subsequently pulled from the market after initially being given FDA approval. Speaking of OxyContin®, Lynch stated "with hundreds dead from overdose and thousands, perhaps, tens of thousands hopelessly addicted." He noted this problem would become worse due to a Federal Appeals Court ruling the patents of Purdue Pharma held on OxyContin® were invalid and unenforceable due to deception by the company in the original application to the patent office. Lynch stated "I find it remarkable that this drug was put on the market without any study pointing to its addictive properties, which leads to the underlying question we have for the FDA and the DEA." He wondered "how addictive will we allow these drugs to become and still be legally marketed." Lynch found it problematic the only recourse upon discovering additional harms associated with a drug is the removal of the drug from the pharmaceutical market. He stated "The story of OxyContin®, its approval from the FDA, its marketing strategy, and its abuse

[86] The reformulation issue continued for some time. A NDA for Remoxy was ultimately rejected and a resubmission will be ruled on by the FDA on June 23, 2011. The FDA requested more proof the drug reduces abuse. Purdue Pharma received approval for a reformulated abuse-resistant version of OxyContin® in April of 2010. In August of 2010, Purdue Pharma ceased sales of the original formulation of OxyContin® and began exclusively selling the new formulation.

and diversion, all illustrate the inability of our current regulatory framework to appropriately address the problem."

As the criticism of Purdue Pharma, the FDA and the DEA reached new levels of intensity, the response began to shift from attempts to make the existing abuse liability system work more efficiently, to a reworking of the system itself. In particular, the abuse liability system began to embrace the concept of "risk management plans" in dealing with potential new drugs of abuse. These plans moved the system beyond informational campaigns like black box warnings on packaging, to more active systems of intervention and response. A critical first step in the process was the development of the RADARS system. By demonstrating a company could, using its own operating capital, develop a reasonably effective system of postmarketing surveillance, Purdue Pharma helped push the abuse liability system toward more comprehensive planning systems for new products. The push for the development of what would become known as Risk Management Plans, or RMPs, was evident at the September 2003 meeting of the Anesthetic and Life Support Drugs Advisory Committee and in a December 2003 GAO report, both of which recommended all NDAs have RMPs as part of the application.

Dr. Robert Meyer (2004), successor to Dr. John Jenkins at the FDA, reported to Congress the FDA would work with individual drug companies to develop "a plan of intervention beyond just labeling to help assure the safe and effective use of the drug." These plans, which the FDA formally began calling risk management plans (RMPs) would henceforth be required in an increasingly large number of cases. "The Agency agrees with these recommendations and believes that it is highly desirable for all

extended release or high concentration Schedule II opiate drug products to have RMPs in place at the time of approval." Meyer noted RMPs would vary depending upon the "safety profile" of medications, but would generally include: identification of appropriate patients, assuring the safe and informed use of the product by both practitioners and patients; and monitoring for adverse outcomes, including misuse, overdose, abuse and diversion. He further noted "FDA plans to provide more specific guidance to the pharmaceutical industry on the development, implementation, and evaluation of RMPs this year" (Meyer, 2004). By 2004, RMPs would also define the parameters of marketing and advertising. Although pharmaceutical companies are allowed to advertise direct to consumers "FDA will continue to encourage sponsors, as part of their RMPs, to voluntarily refrain from advertising directly to consumers as a means to avoid excessive or unnecessary use." A set of guidelines for these plans was published in March 2005 as part of the reauthorization of the Prescription Drug User Fee Act.

Representative Lynch's (2005) invocation of the Palladone® case, ironically, shows the extent of the changes that were made to the abuse liability assessment system in the wake of the OxyContin® case. Palladone® is an analgesic twice as powerful as OxyContin® and approved by the FDA as a 24-hour extended release hydromorphone based medication (Lynch erroneously stated it was morphine based). Palladone®, a product of Purdue Pharma, was given FDA approval on September 24, 2004. The FDA required a black box warning and required Purdue Pharma to produce a risk management plan. On July 13, 2005 Palladone® was removed from the pharmaceutical market. The drug was pulled from the market due to a concern of possible fatal reactions to alcohol. The FDA stated Purdue Pharma did not give

adequate data prior to the approval of Palladone®. Lynch stated a lot could be learned from the experience of OxyContin®, but "it is clear that there is more that can be accomplished through the regulatory process."

Dr. Robert Meyer (2005) noted when the FDA approved the drug Palladone®, there was evidence alcohol could be used to extract hydromorphone from Palladone® capsules. Neither the FDA nor Purdue Pharma anticipated this finding would indicate life-threatening interactions between Palladone® and alcohol. After Palladone® was given approval the FDA received new data indicating "dose-dumping" occurs in patients if Palladone® is taken with alcohol. In a study of twenty-four healthy men concentrations of hydromorphone in the blood were 5.5 times higher when a 12mg Palladone® capsule was taken with eight ounces of forty percent alcohol. Lower concentrations of alcohol showed smaller, but still potentially serious effects on the release of hydromorphone from Palladone®. Based on this information the FDA determined the formulation of Palladone® presented an unacceptable risk and Purdue Pharma agreed to suspend sales and marketing of Palladone®. During questioning, Meyer (2005) stated Palladone® was given the strongest risk management program yet and seemed like a promising medication. The time-release mechanism could not be crushed like OxyContin®. Referring to the "dump-dosing" of alcohol, "it was a regulatory learning from our standpoint that something that in the laboratory could release drug in exposure to high amounts of alcohol could actually do that in the patient setting."

The narrative of the postmarketing response to OxyContin®, then, does not reveal a simple story. The weakness of the existing system generally allowed

OxyContin® to go through the initial approval process, based on questionable analogies to MS-Contin®. In addition, the quality of the postmarketing surveillance system was extremely poor and provided the company and the regulators with delayed data that was generally poor in quality. In the end, Purdue Pharma, the FDA and the DEA initially sought to continue working within the existing regulatory process or try to refine it and make it work more efficiently. The presumptions, particularly with respect to risk-balancing, were not initially questioned by any of the major actors. Not until Congress began to more aggressively challenge both Purdue Pharma and the regulators, did some of the previous assumptions of the abuse liability assessment system change. First, the risk-balancing question began to shift toward preventing drug abuse, as Congress seemed to insist and Congressional hearings gave ample publicity to drug treatment providers and family members of OxyContin® victims. Second, Congress began fundamentally questioning the soundness of the existing system, helping precipitate the initiation of a more formal RMP structure. The Palladone® case actually demonstrates how well that new system could work, catching a previously undetected and never seen before problem of “dose dumping” through alcohol interactions, resulting in the withdrawal of the product from the market after less than one year – a successful case, according to the FDA, of “regulatory learning.”

CHAPTER 7
DISCUSSION

This chapter returns to a consideration of the central organizing questions of this dissertation, discussing the results of this case study and the implications of the findings for the literature on state-corporate crime. This chapter begins with an assessment of whether the abuse liability system failed by allowing OxyContin® to be given FDA approval and in failing to anticipate the dangers associated with OxyContin® abuse and diversion. This chapter then assesses what corporate crimes, if any, were committed by Purdue Pharma and whether the harms caused in this case fit traditional definitions of criminality. This chapter then considers whether the combined actions of Purdue Pharma and the state regulators (particularly the FDA and the DEA) fit accepted definitions of state-corporate crime. This chapter also considers the extent to which "outside" actors and interests groups influenced the process of decision-making in this case and the extent to which this influence might itself influence the assessment of this case study as an instance of state-corporate crime.

Did the Abuse Liability System Actually Fail in the Case of OxyContin®?

Considering whether there was a failure of the abuse liability system is a critical first step. It remains possible the system could have "worked" in the sense that the harms associated with OxyContin® might not have been predictable – they could have been the result, in other words, of unavoidable error. A true failure of the state-corporate abuse liability system, then, would involve some sort of preventable error or delay. Considering the abuse liability system was set up to function both before and after a drug's development and marketing, the assessment must consider the decision-making at multiple points.

One problem with this analysis though is that many of the studies assessing or critiquing the abuse liability system were conducted in part as a result of the problems associated with OxyContin® and these studies were not available during the development and approval of the drug. Animal testing would not have been a perfectly effective means of predicting the subsequent social patterns of use, since animal subject tests were not examining the kind of product manipulations (crushing the release capsule) that allowed for extremely high doses to be received. Wright et al. (2006) noted clinical trials can also be an ineffective in predicting the misuse of drugs because they trials do not allow participants to manipulate the drugs. The first study of the postmarketing surveillance program associated with Ultram® was not published until 1999 (Cicero et al., 1999).

Development and Approval

First, were the potential risks of OxyContin® use sufficiently predictable that these risks should have been foreseen at the drug development and approval phase, resulting in either a denial of the NDA or a mandated reformulation of the drug? Although many seemed to perceive the reformulation of OxyContin® as something of a pipe dream, the FDA gave Purdue Pharma approval for a reformulated abuse-resistant formulation of OxyContin® in April of 2010. In August of 2010, Purdue Pharma ceased sales of the original formulation. In a sense, then, the question here is whether the drug should have been approved in its original formulation at the time or should some effort have been made to insist on a reformulation which eventually did occur fifteen years later?

At the time OxyContin® received FDA approval, both the FDA and Purdue Pharma were aware that crushing the drug would result in a bypass of the time-release capsule. When this was done, up to sixty-eight percent of the medication could be delivered immediately, which would seem to represent a significant defect of the medication. Against this fairly obvious potential flaw, the review of all the available evidence from the FDA suggests the agency accepted four basic premises in support of approving OxyContin®, all of which suggested by Purdue Pharma at the time of the approval process. First, that OxyContin® when used as directed was a safe medication. Second, that most drug users would, in fact use the new drug as directed and that only a relatively small numbers of users would actually crush tablets of OxyContin®. Third, the assumption of small numbers of potential abusers could be safely inferred from the very low numbers of reports of abuse and diversion associated with MS-Contin®. Fourth, the benefits of approving OxyContin® - specifically the addition of an important and effective new analgesic to the pain management field – outweighed the harms associated with low levels of drug abuse.

It is not difficult to see from these four premises the critical role the MS-Contin® analogy played in building a case for FDA approval. From the evidence, it is clear Purdue Pharma put forward MS-Contin®[87] as the primary point of comparison and the FDA accepted this analogy in their decision-making. The use of the MS-Contin® analogy was deeply flawed and led both the company and the FDA to ignore other information, readily available, that might have led them to predict the harms of OxyContin® use. Although both drugs were Purdue Pharma products and both were

[87] Although in one reference the FDA also compared OxyContin® to the drug Duramorph®, another controlled-release morphine which did not have high levels of abuse or diversion.

controlled-release pain medications, these two similarities should not have outweighed two important differences between the two drugs. Throughout the medical literature review[88] and in congressional testimony[89], observers consistently remarked oxycodone produced fewer side-effects and carried less social stigma than morphine. Thus, many correctly imagined OxyContin® would become far more widely prescribed than MS-Contin®. Indeed, Purdue Pharma clearly imagined the same thing, making unprecedented (for that firm) investments in sales and marketing resources. No one seemed to question whether the scale of the new drug's distribution might generate more problems of abuse and diversion.

The more obvious and, ultimately fatal, flaw in the comparison was MS-Contin® could not be crushed in a similar manner to OxyContin®. OxyContin® can work as either a controlled-release drug or if crushed, an immediate-release drug. This reason alone should have prevented any comparison between the two drugs or at least pushed Purdue Pharma and the FDA to consider more germane analogies from recent and more distant past experience. That the analogy was a poor one seems clear and that it derived from Purdue Pharma is also clear. What is not clear at this point in the case study is whether it was offered in bad faith by Purdue Pharma. Though the FDA always acknowledged relying on the analogy, the agency never publicly criticized Purdue Pharma for offering it. On the contrary, FDA administrators from Dr. John Jenkins (2002) to Dr. Robert Meyer (2004, 2005) to Dr. Sandra Kweder (2006) all argued the agency did not believe many drug users would crush OxyContin® pills and all three

[88] See Glare & Walsh, 1993; Kalso & Vaino, 1990; Levy, 1996, 2001b.

[89] Purdue Pharma executives made this claim throughout their testimony. Dr. Michael Levy (2001a), Dr. Janet Abrahm (2005) and Dr. Robert Meyer (2004, 2005) of the FDA made this claim as well.

stated flatly that the dangers associated with the drug were unexpected and unforeseen.

Nonetheless, if the position was genuine, it was naïve at best and negligent at worst. The release of OxyContin® to the pharmaceutical market represented the highest amount of oxycodone available in any formulation. Furthermore, OxyContin® was pure oxycodone, so a drug user did not have to worry about ingesting too much acetaminophen, ibuprofen or aspirin, which is added to many other forms oxycodone-based drugs. Representative James Greenwood (R – Pennsylvania) (2001) referred to OxyContin® as the "jet fuel" of the drug world. Even keeping hindsight in mind, it is hard to believe this was not realized quicker and drug users would seek out the most potent synthetic opioid available at the time. Additionally, although many blamed the warning to not crush OxyContin® pills as an advertisement to do so, it is a near certainty drug users would have figured this out without the warning label.[90]

As many of the interviews and congressional testimony noted, drug users have a long history of creative manipulations of drug products. Rick Hall (2001), a Captain in the West Virginia State Police, testified observing drug users (prior to OxyContin®) opening capsules of Tylox and snorting or injecting the oxycodone found within. E. Leong Way mentioned Benzedrine inhalers, which could be broken open and the amphetamine paper stripped out. Sidney Schnoll discussed at length the T's and blues phenomenon. Users of this concoction took the creative action of crushing a narcotic pill and mixing it with a separate crushed antihistamine. If drug users could think of

[90] Dr. Rory Sullivan (2001), a Director of a West Virginia rehabilitation clinic argued the warning against crushing OxyContin® actually served as an advertisement for drug addicts to do so.

these creative ways to misuse drugs (and countless others not mentioned), perhaps Purdue Pharma and the FDA should have known this was a possibility with OxyContin® as well.

When defending the decision to approve OxyContin®, Jenkins (2002), Meyer (2004, 2005) and Kweder (2006) all stated the medication was safe when it was used as directed. The FDA, representatives from Purdue Pharma and many medical practitioners stated when patients are properly treated, addiction is rare and patients who need pain medications should not be considered addicts. Dr. Michael Levy (2001a) argued these patients should not be considered different from diabetics who need insulin. Several medical practitioners stated OxyContin® was one of the most important analgesics to be introduced to the pharmaceutical market since MS-Contin®. Many considered OxyContin® the next step in pain management. Levy (2001a) went so far as to say OxyContin® had "the characteristics of an ideal opioid." Even if medical practitioners did not go that far in their endorsements of OxyContin®, many argued pain management requires a variety of drugs for the individualized treatment of patients and a controlled-release form of oxycodone was an important addition to the analgesic pharmacopeia. Dr. Janet Abrams (2005) argued more than ibuprofen and acetaminophen was needed to treat cancer patients and stated several of her patients could only be treated with OxyContin®.

Although the argument that OxyContin® is safe when used as directed is compelling, there are problems with this assertion as well. The original warning label failed to mention the risks associated with OxyContin®; this oversight (one could argue deliberate by Purdue Pharma) was corrected by the revised black box warning in 2001.

Dr. David Egilman (2004) stated this was particularly troubling considering the warning label of MS-Contin® always contained a warning against abuse and of a potential for addiction. This was somewhat ironic considering MS-Contin® turned out to be a far less abused drug. Many people argue OxyContin® should have been only approved for the treatment of severe pain and not moderate to severe pain. Dr. Rory Sullivan (2001) argued prior to the release of OxyContin® there were already many effective treatments for moderate pain. He believed many physicians prescribed OxyContin® for osteoarthritis or back pain when other medications would have been more appropriate. Dr. Michael Levy (2001a) argued though such prescription practices by physicians had been altered because many physicians were unwilling to prescribe morphine to patients for these types of ailments.

The DEA and FDA took opposing viewpoints on the approved usage of OxyContin® at the February 2004 hearing with the DEA arguing OxyContin® should only be approved for the treatment of severe pain and the FDA arguing OxyContin® should be approved for moderate to severe pain. Dr. Meyer (2004) noted, pain is not typically monotonic and can wax and wane. Therefore, a patient may one day be in moderate pain, but severe pain the next day. He followed up this point by noting OxyContin® was an inappropriate medication for pain that needed to be treated "as needed." The sentiment of the FDA seems valid in one sense that patients should not have to worry about being undertreated for pain, but the position would also seem to allow for the possibility that on some days a patient may be taking more pain medication than they need. Furthermore, the label does not state OxyContin® is approved for patients who suffer from pain that varies between moderate and severe pain. Thus, a

patient who will only suffer from moderate pain would be approved to take OxyContin®. Frederick Pauzar (2004) and Marianne Skolek (2007) testified Pauzar's son and Skolek's sister were prescribed OxyContin® when a lower-strength opioid would have been more appropriate. Both their family members died of drug overdoses.

Another problem is establishing what should be considered moderate pain. This definition could vary between patients and physicians considerably. Dr. Michael Ashburn (2001) stated "only a qualified physician, together with his or her patient in the context of a doctor-patient relationship, has the information necessary to decide what approaches, structure and therapeutic goals are appropriate for the management of pain in a particular situation." Although this might work for pain management specialists and oncologists, many witnesses stated pain management is specialized training many physicians lack. Approving OxyContin® for only serious pain would not prevent physicians from prescribing the drug for moderate pain; it would have only prevented Purdue Pharma from marketing the drug for moderate pain. If physicians discovered OxyContin® was appropriate for moderate pain, they could prescribe the medication in that manner. But instantly approving the most potent form of oxycodone for moderate pain might not have been the best way to market the drug upon it first being introduced to the pharmaceutical market. It seems like a more cautious approach should have been taken.

Although the FDA stated OxyContin® was safe when used as directed, it seems the more compelling reason OxyContin® was approved was the FDA concluded the benefits of approving OxyContin® outweighed the risks associated with the drug. From the first hearing to the last, members of Congress and drug regulators repeatedly stated

it was important patients in pain had access to the proper pain medications. Many of the witnesses expressed hope or frustration OxyContin® would be reformulated, noted the needed for more prescription monitoring programs, blamed Purdue Pharma for aggressively marketing the drug, but only Rick Hall (2001) of the West Virginia State Police,[91] Dr. Art Van Zee (2002),[92] Steven Tolman (2005) (a Massachusetts State Senator), Brian Wallace (2005) (a Massachusetts State Representative)[93] and Barbara Van Rooyan[94] (2006) (who lost her son to OxyContin® use) supported removing OxyContin® from the pharmaceutical market. The needs of patients in pain always trumped the need to prevent people who abused and diverted OxyContin®. Thus, it seemed like taking OxyContin® off the pharmaceutical market was never an option seriously considered.

Postmarketing Surveillance and Policy Response

Perhaps the greatest lesson learned from the regulatory experience with OxyContin® is the gross inadequacy of postmarketing surveillance. This was a common theme among witnesses, both expert and in congressional hearings. Cicero noted the FDA and pharmaceutical companies seemed to have petty disputes throughout the drug approval process that were more about posturing and power than about the actual science or data being considered. According to him, once a drug was

[91] Hall argued any patient who was in enough pain to require OxyContin® should be treated on an inpatient basis in a hospital.

[92] Van Zee stated OxyContin® was too potent to be on the pharmaceutical market at that time, but did not specifically state what needed to change to allow the drug on the market.

[93] Both state legislators had supported bills in Massachusetts to ban OxyContin®. Neither seemed to express hope a ban would be successful. Tolman stated “the bill has proven controversial, but it has caught people’s awareness, and most importantly it’s becoming more prevalent we have a very serious epidemic on our hands.”

[94] Van Rooyan supported a recall of OxyContin® until the drug could be reformulated.

approved both the FDA and pharmaceutical companies seemed to take for granted the drug was safe and were not interested in doing follow-up studies until reports of harm and/or death surfaced. Dr. Jack Henningfield (2004) noted such a situation would not be acceptable if the CDC took two, three or more years to identify diseases such as SARS or West Nile. The first three congressional hearings, which all took place within five years after OxyContin® was given FDA approval, were primarily concerned with determining if OxyContin® abuse and diversion were problems and how large the problem was. Members of Congress continually asked what data witnesses had and the common response was more data needed to be collected. Throughout the entire seven hearings the questioned that never seemed to be adequately answered was how much harm OxyContin® caused.

The GAO report included a very pointed criticism of postmarketing surveillance; noting the reporting services such as DAWN, NSDUH and Monitoring the Future "all have limitations that prevent an assessment of the relationship between the availability of OxyContin® and areas where the drug is being abused or diverted. Specifically, these databases, which generally do not provide information on specific brand-name drugs such as OxyContin®, are based on data gathered from limited sources in specific geographic areas and have a significant time lag. As a result, they do not provide reliable, complete, or timely information that could be used to identify abuse and diversion of a specific drug" (GAO, 2003, p. 32). As Lloyd Johnston (administrator of Monitoring the Future) noted, the annual survey will add new drugs to the survey after receiving initial information about problems associated with the drug. Usually it will began with adding one question concerning the drug and adding successive questions

each year if the drug appears to be a problem. Although this allows Monitoring the Future to track drug use over time, it will only include timely information for drugs that have been a problem in previous years. It could take years to establish the amount of abuse associated with a new drug and the survey might only catch a second wave of abuse, but most likely not the first wave.

As Cicero and Schnoll note, perhaps the first true postmarketing surveillance assessment was conducted with the drug Ultram®. This was an unusual case because the manufacturer of the drug convinced the FDA to refrain from scheduling a narcotic based upon data from Europe showing low reports of abuse and diversion and a promise by the manufacturer to commit to postmarketing surveillance of the drug. This plan began in 1995, the same year OxyContin® was given FDA approval. When the FDA required Purdue Pharma to develop a risk management plan in 2001, Purdue Pharma hired Cicero and Schnoll (and several renowned researchers as well) to develop the RADARS system which relied heavily on the researchers experience with Ultram®. Subsequently, the FDA released guidelines for future NDAs to include risk management plans if the unapproved drug might have abuse potential.

Although the RADARS system was certainly a step in the right direction, the endeavor did not provide a definitive answer to questions about OxyContin®, even among two of the researchers responsible for developing the program. Cicero came to the conclusion OxyContin® was every bit the “problem drug” critics claimed and Cicero essentially blamed Purdue Pharma for creating the prescription drug crisis by the aggressive marketing campaign the company promoted for OxyContin®. Schnoll came to the conclusion abuse of OxyContin® was highly regionalized and typically occurred in

rural areas where the supplies of heroin and other drugs were typically low. It seems no matter how much data exists, interpreting the results will always be open to debate, even among experts.

If the basic postmarketing surveillance system was deeply flawed, what about the timeliness and quality of the response to the reports of abuse that *were* generated? OxyContin® was introduced to the pharmaceutical market in December of 1995. Rick Hall (2001) stated he observed abuse and diversion of the drug in 1998, but most witnesses (including Purdue Pharma, the FDA and the DEA) stated they first heard reports in late 1999. In February of 2000, former U.S. Attorney Jay McCloskey (2007) sent a letter to Purdue Pharma in which McCloskey relayed his concerns about the abuse and diversion of OxyContin® in Maine. Purdue Pharma requested a meeting the following month, but McCloskey deferred until later in the year. By the end of 2000, Purdue Pharma had met with McCloskey and the FDA regarding abuse and diversion. In 2001, Purdue Pharma had begun many of the educational efforts cited in the results, the company voluntarily removed 160 mg dosages of OxyContin® in April and in July Purdue Pharma and the FDA had developed a new warning label for OxyContin®. In that same year, Purdue Pharma and the FDA coordinated to develop a risk management plan for OxyContin® and on August 28, 2001 the first of seven congressional hearings was held. Furthermore, many of the lessons learned from OxyContin® (such as risk management plans) were incorporated into permanent FDA policy.

Critics of the FDA and the pharmaceutical regulatory process may argue prescription drugs had been a problem for quite some time and the agency should have

been better prepared for the problems OxyContin® caused. However, whether OxyContin® really should be considered a problem drug or it was the subject of a moral panic, it seems clear OxyContin® was the proverbial straw that broke the camel's back and served as the catalyst behind many long overdue changes in regulatory policy. Although it might be an unfortunate comparison, considering OxyContin® is a very useful analgesic and is safe when used as directed, the drug might be compared to thalidomide[95] or elixir of sulfanilamide for ushering in much needed change in pharmaceutical regulation. Historically speaking, a problematic drug or class of drugs has always been the catalyst for change. Keeping this in mind, one might say the response of the FDA was actually fairly swift. Laws such as the Pure Food and Drug Act (and subsequent amendments to the law), the Harrison Narcotic Act and the CSA were passed after years of effort and lobbying. The FDA, by enacting guidelines for risk management plans and requiring them for NDAs in the future, saw shortcomings in the process and remedied them without new legislation having to be enacted.

Were Corporate Crimes Committed?

The legalistic answer to the question of whether corporate crimes were committed is yes, since three executives and the company itself reached a plea agreement with federal prosecutors in which they pled guilty to misbranding the drug, for which they were required to pay millions of dollars in fines.[96] The 2007 plea agreement, reached with John L. Brownlee, the United States Attorney for the Western District of Virginia, hardly satisfied the critics of Purdue Pharma. Indeed, the plea

[95] Although thalidomide has been given FDA approval for other uses than it was originally intended.

[96] "Misbranding" of a drug refers to any mislabeling of a drug product or fraudulent promotion and marketing of a drug.

agreement itself became the subject of yet another congressional hearing, during which several senators questioned why the three executives or anyone else employed by the company did not receive jail time and why no employee was convicted of anything beyond a misdemeanor. Senator Arlen Specter (2007), for example, believed the actions of Purdue Pharma might have warranted a prosecution for second degree murder or involuntary manslaughter. For his part, however, U.S. Attorney Brownlee (2007) argued to the senators the case was complicated and it could not be proven beyond a reasonable doubt any employee of Purdue Pharma had specific knowledge of any intent to deceive consumers. Brownlee stated knowledge could be imputed to the corporation, but not to any one individual.

The cautions of Brownlee to the Senate committee speak directly to the criminological question at hand – can this case study be held up as a case of corporate crime? Many aspects of the case of Purdue Pharma and OxyContin® are reminiscent of the debate between Sutherland and Tappan that took place so many years ago. Sutherland, taking his "big tent" approach to the definition of corporate crime, would have surely condemned the false advertising of Purdue Pharma and then would have most likely made the argument Purdue Pharma had engaged in socially injurious behaviors that had caused a great deal of harm. These actions were the result of corporate greed to maximize profit with little regard to the safety of consumers.

On the other hand, Tappan would have most likely noted that Purdue Pharma might not have been the most socially responsible actor, but except for the false advertising (which was a strict liability offense that required no proof of *mens rea*), Purdue Pharma had not committed any criminal actions. The company aggressively

marketed OxyContin®, but that should be expected from any company selling a drug with a limited patent. Furthermore, Purdue Pharma lacked the *mens rea* to specifically harm anyone. Although OxyContin® had a design defect, it took the intervening action of a motivated person (either a recreational user or a drug addict) to misuse the drug. Purdue Pharma specifically warned against this practice and company employees repeatedly stated they did not want their product to be misused in this manner. This case study, I argue, tends to offer support for taking the Sutherland approach to corporate crime.

Purdue Pharma, intentionally or not, relied on highly misleading analogies with MS-Contin® to argue prospectively for the safety of OxyContin®. It also argues that, even if the corporation was not deliberately attempting to deceive the FDA, its own preapproval assessment of the potential for abuse of OxyContin® underplayed obvious potential problems. Even more to the point, one of the critical differences between MS-Contin® and OxyContin® was the size and scope of the two drugs' marketing and distribution – a difference directly attributable to the decision of Purdue Pharma to invest what were for the company unprecedented resources into promoting sales of OxyContin®. This corporate decision-making seems directly connected to the eventual social harms that occurred from users manipulating the formula of the drug to access higher dosages of oxycodone.

Can this decision-making be imputed to the corporate organization itself, as traditional definitions of corporate crime would look for? Here, the answer seems to be that it can, more so than some other recent case studies critical of the search for corporate *mens rea*. The work of Lee and Erdmann on the Ford Pinto case, for

example, provides an excellent caution about corporate decision-making, arguing in that case the complexity and size of the Ford Motor Company prevented any unified plan of decision-making that would easily fit a corporate crime mode. In this case, by contrast, Purdue Pharma present a far simpler organization structure, one in which it would be far less likely for decisions to be made without full awareness within the company. This hardly amounts to a rejection of the Pinto studies; rather, it indicates that not every corporate decision-making structure will have the complexity of that case, and that certain product development environments will actively work to integrate decision-making.

Purdue Pharma is a privately held company, owned by the Sackler brothers and headquartered in Stamford, Connecticut. Purdue Pharma has laboratories in Cranbury, New Jersey and manufacturing facilities in Wilson, North Carolina, Totowa, New Jersey and Coventry, Rhode Island. According to Meier (2003), from 1952 to 1987 Purdue Pharma was run by one man, Arthur Sackler. Since Arthur's death, in 1987, the company has essentially been left to his brother Raymond to manage while his brother Mortimer manages the European wing of the corporation, Napp Pharmaceuticals. Meier notes "In 1952 the Sacklers acquired a firm that was barely more than a shell company, with annual revenues of only $22,000" (Meier, 2003, p. 208).

All three brothers graduated from medical school and practiced as clinical psychologists. Among them Arthur was the oldest, and in some ways, more of a father than a brother to his younger siblings. Arthur was a dominant figure in the pharmaceutical company, not just as a manufacturer of drugs, but as a lobbyist and

researcher as well.[97] Meier seems to imply Arthur Sackler was to the pharmaceutical industry what Joe Kennedy was to Wall Street; wildly successful but excessively prone to rule breaking. In 1962, Arthur Sackler was called to testify before a U.S. Senate Committee hearing chaired by Estes Kefauver investigating misleading and deceptive advertising by the pharmaceutical companies. Sackler walked away from the hearing without being harmed by the process. It was not until after his death, upon the settling of his estate, that it was revealed how extensive his power within the pharmaceutical industry actually was (Meier, 2003). Relative to the largest international pharmaceutical firms, Purdue Pharma is modest in size, with 1,000 employees at its Connecticut headquarters and 2,200 additional employees distributed among its four other facilities.

It is not simply organizational size and structure that suggests Purdue Pharma executives had a shared understanding of corporate decision-making; the particular nature of the regulatory system in the case of the drug industry would have compelled this in any event. Unlike the Ford Motor Company and sales of the Ford Pinto (or any other automobile for that matter), Purdue Pharma was not allowed to sell a single tablet of OxyContin® without government (FDA) approval. Hawthorne (2005) notes that FDA approval for a drug can take years of work. The rigorous approval process requires that the corporation provide all information describing the medication's safety and effectiveness during clinical trials.[98] Not only must this information be made available to the FDA at all times during the approval process, it must be presented in coherent,

[97] Meier (2003) argues much of the research pushed by Arthur Sackler was propaganda for his advertising clients.

[98] See Chapter 3.

organized and complete detail.[99] Pharmaceutical companies will remain in constant contact with FDA officials throughout the approval process and if an employee does not possess the information they need regarding a drug pending approval, this information should not be hard to find.

In assessing the actions of Purdue Pharma, it is important to observe the company operated within an abuse liability assessment system that placed much of the responsibility for research and evidence on the company itself. Not only would the company have been well aware of that responsibility, but the company was well established in the field of pain management and opiate analgesics. In addition to OxyContin®, Purdue Pharma sells: Butrans® (a transdermal patch containing buprenorphine, a Schedule III drug which required a separate federal law allowing it to be prescribed for the treatment of opiate addiction), Dilaudid® (hydromorphone, a Schedule II drug many witnesses referred to as "drugstore heroin"), MS-Contin® (controlled release morphine and a Schedule II drug) and Ryzolt® (extended release tramadol, the base drug of Ultram®, which was the subject of the first true postmarketing surveillance program). Including OxyContin®, three of these five drugs are recognized as having a very high potential for abuse and Butrans® is in a schedule of drugs recognized as having a high potential for abuse. Each drug has a strict warning label which advertising or marketing should not deviate from or minimize. It was noted in testimony by both Michael Friedman (2001) and Paul Goldenheim (2001, 2002) Purdue Pharma began developing pain medications in the early 1980s and as

[99] Hawthorne (2005) recounts the drug Erbitux®, developed by ImClone and most commonly associated with Martha Stewart, was denied FDA approval the first time for providing incomplete information in its NDA.

1984 began to place the company in the position of providing information to medical professionals regarding the appropriate and responsible prescription of opioids.

In fact, Purdue Pharma continually presented themselves as experts in pain management. Although one could quibble with this self-proclaimed designation, for purposes of assessing corporate crime, this admission of knowledge is important for this analysis. What this case study clearly shows is Purdue Pharma was well aware of the limitations of the abuse liability assessment system – by their own statements they were aware prescription drug monitoring systems were not terribly effective, the existing postmarketing surveillance system was deficient, medical professionals needed more and better training in pain management and drug treatment systems were underfunded – and despite this, Purdue Pharma chose to pursue an aggressive strategy of marketing and promotion for which the existing system was not well prepared. The decision to push OxyContin® into a regulatory environment ill-equipped to monitor or respond to potential problems echoes Sutherland's earliest criticisms of the drug industry in which he argued the industry wanted a weakened regulatory. The company decided to aggressively market what should have been perceived as an attractive drug to recreational users in a regulatory climate Purdue Pharma continually stated was unequipped to properly deal with the existing analgesic pharmacopeia, much less the most powerful form of oxycodone yet introduced. Not until 2001 did the company finally begin to respond to the deficiencies of the existing system (with, for example, the initial investments in the RADARS system) rather than taking advantage of those deficiencies.

Beyond the general corporate level of responsibility for over-aggressive promotion, there are more specific questions of criminal actions in advertising and

promotion. At the first Congressional hearing, Michael Friedman (2001) seemed to take responsibility for the actions of Purdue Pharma. During his testimony he stated “My responsibilities at Purdue include the direct oversight and management of sales, marketing, human resources, licensing, and business development.” The sales division of Purdue Pharma employed 318 people in 1996, 319 in 1997, 377 in 1998, 471 in 1999, 671 in 2000, 766 in 2001 and 767 in 2002. Through a co-promotional agreement with Abbott Laboratories, Abbott provided 300 sales representatives to Purdue Pharma in each of those years; not an exceedingly large amount of people to manage. According to Purdue Pharma, to begin employment in the sales division of the company, an employee must complete a thirty-six week training course. As noted previously, the advertising industry has consistently been rife with everything from slight puffery to outright false claims (GAO, 2003). In some industries misleading advertising might be considered the norm and in the greater scheme of things is probably not a big deal; however, that should not be the case with pharmaceuticals.

The advertising of drugs is regulated by federal law. Therefore, when Purdue Pharma stated OxyContin® was less abusable or less addictive than other medications, the company should have been able to produce data supporting these claims. Mere speculation based upon the previous experience with MS-Contin® or a belief (which turned out to be mistaken) controlled-release drugs are less abusable than immediate release drugs should never have been considered justifiable support for these claims. When asked the question of why the federal government did not prosecute any individual sales representatives, Brownlee (2007) responded proving what any individual representative had stated would be difficult and representatives could use the

charts and graphs depicting the low abuse potential of OxyContin® as proof they were merely following corporate instructions. It is extremely curious why Brownlee did not use this defense of sales representatives as evidence of a corporate policy that violated federal laws regulating the advertising of pharmaceuticals. If Friedman's admission of his oversight duty was not enough and he did not officially sign off on the very deliberate advertising campaign, someone within the corporation had to. Promotional aids could not have simply appeared out of thin air.

Considering sales representatives who did not market OxyContin® appropriately, an analysis of this wrongdoing is not exceedingly difficult. Although a sales representative can provide journal articles or other credible studies illustrating off-label use, sales representatives are supposed to confine their promotion to individual medical practitioners to the approved usages of a drug. If there was a policy in place, in particular if the thirty-six week training course instructed sales representatives to deviate from the warning label on OxyContin®, this would be evidence against Purdue Pharma the company encouraged employees to mislead medical practitioners. If that was not the case and instead the bonus structure for sales representatives of Purdue Pharma and a loose supervisory environment encouraged sales representatives to deviate from the acceptable advertising practices then sales managers and corporate executives had a duty to change this culture.

If Purdue Pharma had wanted to be able to play fast and loose with advertising rules, the company should have stuck with selling antiseptics and laxatives. When Purdue Pharma made the decision to enter pain management, they willingly entered into a new branch of the pharmaceutical market that had stricter rules and regulations.

The company was cited six times by the FDA for their promotion of MS-Contin® by making unsubstantiated claims of superiority. Instead of learning a lesson from these rebukes; the company went further in their disregard for the rules with the marketing of OxyContin®. Although Purdue Pharma would often blame the inadequacies of government oversight and regulation for allowing harm to occur, the company routinely disregarded these inadequacies by aggressively marketing OxyContin® and disregarded the rules regarding the proper advertisement of their product as well.

State-Corporate Crime

At the heart of much of the literature on state-corporate crime is the idea that individual corporations or entire industries benefit from the absence of appropriate state regulation, or from lax or excessively deferential state regulation – and that, at the heart of this, is a kind of mutually beneficial arrangement in which both state and corporate interests benefit. For example, Aulette and Michalowski (1993) argued that the fire at an Imperial Food Products chicken-processing plant in Hamlet, North Carolina was causally linked with the state's deferential approach to the manufacturing industry. Additionally, the state's Occupational Safety and Health Program failed to properly monitor the safety conditions at the production plants, thus essentially allowing for the hazardous conditions preceding the fire. Matthews and Kauzlarich (2000) argued the FAA did not adequately enforce safety regulations which led to the dangerous conditions that caused the crash of ValueJet Flight 592. Similar to these two examples, it certainly is not hard to see a similar state of affairs in the poor state of state regulatory capacity with respect to the drug industry. As this study has shown, the drug industry has often been poorly regulated. It took decades simply to pass a federal law which

only required drug makers to truthfully list the ingredients contained in medications. New bursts of legislative enactments tended to lag well behind their perceived necessity and generally happened only in the wake of widely publicized system failures (like the thalidomide case).

Robert Balster, a former chair of the FDA Advisory Committee stated the abuse liability system worked “pretty good” and he stated “there have not been a whole lot of really serious misses.” In fact, he argued just the opposite of what many critics of the abuse liability assessment system have argued – Balster stated the FDA had a tendency to over-regulate. Ted Cicero described the relationship between the pharmaceutical industry and the FDA as divisive and noted the two sides would often conflict with each other out of habit rather than purpose. He stated the FDA had taken several steps to improve risk management and should avoid the temptation to over-schedule drugs.

When considering if the current case study of OxyContin® represents a state-corporate crime, it is important to analyze the actions of the state and determine the complete context of the failures of the abuse liability system. This process begins with the initial decision by the FDA to approve OxyContin®. Several critics questioned the FDA about the initial approval of OxyContin®. Specifically, if the ease of bypassing the time-release capsule should have been considered a fatal flaw and if the agency should not have approved the drug until this defect was fixed or a version of OxyContin® containing an antagonist was released. The FDA took the position if OxyContin® was used as directed it was a safe and effective medication. Furthermore, FDA stated the agency did not have the authority to direct a company to develop a new medication; the

agency only evaluates the safety of drugs submitted to the agency for approval. The FDA stated beyond placing a warning label on medications, the agency was not allowed to place other restrictions on approved medication unless it was part of federal legislation such as methadone and buprenorphine programs. Restricting which physicians could prescribe OxyContin® was not an option because the agency was not allowed to regulate the practice of medicine; that duty is left up to the individual states. Dr. Jenkins (2002) argued if the agency tried to take any of these actions it would set an extremely dangerous precedent. Thus, in some ways federalism might be considered a culprit in this case of regulatory failure.[100]

In addition to the state actions that led to the approval of OxyContin®, was the decision that led to the original label for the drug. Many critics of the FDA stated the agency should not have approved the original warning label for OxyContin®[101] which did not warn of the potential for abuse and addiction associated with the drug. Meier (2003) indicated the FDA had been essentially duped by Purdue Pharma and the omission in labeling served as a de facto endorsement of the advertising claims of Purdue Pharma. However, this conclusion is incorrect. Federal pharmaceutical advertising rules prevent manufacturers from making claims not supported by data. Therefore, even if there was an omission on the label of OxyContin®, this omission still did not allow Purdue Pharma to make the claims they were eventually punished for. The FDA may have presented an opportunity for Purdue Pharma to mislead consumers,

[100] This would certainly not be the first time federalism has caused inadequacies in regulation. Some of the earliest examples include the rationale for the Articles of Confederation, opposition to the ratification of the United States Constitution, Thomas Jefferson's fight to eradicate a national bank and the American Civil War to name a few.

[101] Perhaps most forcefully by Dr. David Egilman (2004).

but the agency certainly did not endorse such a position and as Purdue Pharma found out later when it pled guilty to misbranding OxyContin®, their actions were not legal.

Another deficiency of the abuse liability system, which many cited as one of the biggest problems that allowed prescription drugs to be abused and diverted was the lack of prescription monitoring program. Former Deputy Director of ONDCP Dr. Bertha Madras (2006) noted in 2000 only fifteen state programs were in place, but by 2006 thirty-three state programs were in place. According to the DEA Office of Diversion Control,[102] currently thirty-four states have programs and seven states have enacted legislation for programs, but they are not yet operational. The state of Washington decided to temporarily suspend their program due to budget cuts. Much like the regulation of the practice of medicine, this is a state responsibility the federal government can only encourage the states to establish. The federal government did that by passing the Harold Rogers Prescription Drug Monitoring Program which provides funds to individual states to establish these programs. This is an issue of federalism, not of inaction by the federal government. Thus, after identifying a problem, both the federal government and many individual states took action to fix the problem.

Although there are a number of elements to the OxyContin® story that suggest the state holds some responsibility for the social harms resulting from the drug's widespread marketing, not every element to the story fits neatly within the state-corporate crime paradigm. For one, there is clear evidence that the regulatory system took on appropriate adaptations in the wake of the OxyContin® case; indeed, initiated them in the midst of the case. The FDA and the company collaborated on the

[102] See http://www.deadiversion.usdoj.gov/faq/rx_monitor.htm

development of the RADARS system, which in turn led to a more systematic approach being adopted by the FDA toward the requirement of formal risk management plans.

Although the FDA stated the agency had taken actions similar to risk management plans in the past, OxyContin® had the distinction of having the first FDA-mandated risk management plan. After this experience, the agency stated it would require all pharmaceutical companies filing NDAs to have a risk management plan if the proposed drug had abuse liability. When Palladone® was briefly approved, the FDA gave the drug the strictest risk management plan the agency had ever required and the drug was pulled from the pharmaceutical market not based upon reports of harm, but based on potential harm from controlled tests. The agency noted a dose-dumping problem was identified when the drug was mixed with alcohol. The FDA had not previously encountered such a problem with a drug, but did not use the same refrain with OxyContin® that Palladone® was safe when used as directed. Although a cynic might state the FDA did not simply want to suffer another public relations hit, nevertheless, the agency enacted new policy and used it. As a result, a very promising and potentially lucrative drug was taken off the market. If the FDA and Purdue Pharma were either collusive actors or if the regulatory agency was too deferential a pharmaceutical company this would not have happened.

These actions are balanced by some lingering limitations in the regulatory system. A clear instance of regulation deficiency appears in the case of the FDA's oversight of pharmaceutical advertisements. FDA regulation of advertising continues to be conducted post hoc. Whenever a pharmaceutical company advertises a drug, the only requirement is that a copy of the advertisement be filed with the FDA at the time

the advertisement is disseminated; the FDA does not have to give prior approval of these advertisements. Like any state or federal government agency, the FDA continually states it is underfunded or understaffed. In some instances, an advertisement will not be reviewed until a year or more after the advertisement has been viewed by potential consumers. The most common penalty for offending advertisements is a warning letter requiring cessation of the advertisement or a subsequent corrective advertisement. According to the testimony of Dr. John Jenkins (2002), the agency sends out approximately one hundred letters a year. Such a policy does not exactly encourage pharmaceutical companies to comply with advertising requirements and could have possibility led to a belief among pharmaceutical companies they should advertise their products as they see fit and then just apologize if caught. If the FDA changed their policy so advertisements required prior approval of advertisements this climate might change. If pharmaceutical companies complained this process was too slow, then perhaps the agency might change to a policy of requiring preapproval of Schedule II or Schedule III drugs or making some other type of priority system so drugs that might cause some danger (if not used as directed) had more stringent marketing restrictions.

Another critical limitation of the existing system is the capacity for monitoring drug prescriptions and the gray market in pharmaceuticals. The current drug control apparatus was designed to evaluate the safety of drugs and then determine the legal status of each drug. What happens after that is often clearly deficient; there is far less capacity for tracking the medical us (and abuse) of drug products than one would ideally want in order to maximize control efforts. Of course, this deficiency reflects the ongoing

struggle to define the appropriate balancing of costs and benefits. On the one hand, the benefits to more closely tracking postmarketing drug distribution would presumably follow from reduced drug abuse. On the other hand, pursuing prescription drug diversion cases is difficult and labor intensive. Furthermore, it is dependent upon many medical practitioners to evaluate patients to see if they are seeking legitimate prescriptions. Such a situation can breed mistrust into relationships (such as doctor-patient) which many would consider sacrosanct. Additionally, society tends to think of illegal drugs as much more dangerous than prescription drugs. Thus, most of the resources allocated to regulating drugs are dedicated to policing illegal drugs.

An additional complication the state-corporate crime paradigm fails to account for is the multiple interests and parties within the state. Drug approval is determined by the FDA, but enforcement of federal drug laws is left to the DEA. Throughout the hearings these two agencies were not always in agreement, especially about the approved usage for OxyContin®. At the September 2005 hearing, Representative Candice Miller (R – Michigan) noted the FDA and DEA had different interests "but then there are also times when the FDA and the DEA would benefit from a stronger relationship." Furthermore, ONDCP, NIDA and SAMHSA are additional federal agencies responsible for creating drug control policy. All five of these agencies have different agendas and priorities. Such a diffusion of controlling authority hardly accounts for a monolithic state presence.

A further complication of the process that occurred was the presence of Congress. Initially, most members of Congress seemed to be friendly to the bureaucratic agencies, but that patience appeared to wear thin. At the February 2004 hearing, Representative Mark Souder (R – Indiana), when he was not obtaining

answers he found satisfactory, asked two law enforcement witnesses “How many people have to die and at what level does OxyContin® have to become a problem here in central Florida, and Florida, before it becomes a part of a HIDTA request or a DEA request?” At the same hearing Representative John Mica (R – Florida) (2004) stated by the time information became available the information was old and deaths had already occurred. He believed federal law enforcement was not doing enough to solve the problem. At the September 2005 hearing, Representative Stephen Lynch (D – Massachusetts) asked “how addictive will we allow these drugs to become and still be legally marketed?” He further stated “The story of OxyContin®, its approval from the FDA, its marketing strategy, and its abuse and diversion, all illustrate the inability of our current regulatory framework to appropriately address the problem.” At that hearing, both Lynch (2005) and Representative Miller (2005) would chastise both the FDA and DEA for falling to provide any recommendations for new legislation to the hearings. At the July 2006 hearing, Representative Souder stated he was “tired of the empty rhetoric and long delays on important matters like this.” He noted the DEA often took too long to provide information to Congress and a recent synthetic drug action plan “Despite being 20 months in the making, this strategy is full of platitudes that don’t seem to be truly backed up with any assigned responsibility or interim goals prior to the end of this administration.”

Although frustration by members of Congress seemed to be present throughout the hearings, not all members were unanimous in their condemnation of federal agencies. As previously mentioned, several of the members of Congress urged balance and noted they had family members who had died horribly from undertreated

pain. Additionally, several members of Congress[103] were physicians and routinely stated the current regulatory climate was a vast improvement from previous times when pain medication was often unavailable. In addition to these arguments were others from members of Congress[104] that illegal drug use had always been a problem in their districts, but no one seemed to care until prescription drugs became a problem. Perhaps the only member of Congress that really might fit the mold of a state-corporate crime figure would be Senator Christopher Dodd (D – Connecticut) (2002). However, the duty of a member of Congress is to represent their state and their constituents. In some ways, had he not provided a spirited defense of Purdue Pharma he would have been derelict in his duty to the citizens of Connecticut.

Third Parties

One of the problems with the state-corporate crime paradigm is it assumes a binary relationship between corporations and regulatory bodies. Essentially, these two parties are working in tandem for the benefit of both parties to the detriment of ordinary citizens. Although researchers of state-corporate crime have presented compelling cases of this process, these analyses are often too simplistic and forget to account for other actors in the process and what affect these parties might have on the process.

When Matthews and Kauzlarich (2000) considered the crash of ValueJet Flight 592, the researchers blamed ValueJet, SabreTech and the FAA for creating the circumstances through which the plane crash occurred. Yet, no consideration was given to consumers who wanted cheap plane tickets. Although few of the passengers

[103] Representatives Charlie Norwood (R – Georgia) (2004), Dave Weldon (R – Florida) (2004) and Tom Coburn (R – Oklahoma) (2007) also mentioned their individual experiences as physicians.

[104] Representatives Jose Serrano (D – New York) (2001) and Elijah Cummings (D – Maryland) (2006) both made this argument.

probably knew the extent to which the flights were dangerous, at least some passengers might have considered a company called ValueJet probably cut a few corners. Furthermore, it is extremely likely many consumers did not purchase tickets from ValueJet because they believed cut-rate air service was not a good bargain or worth the risk. When considering the Ford Pinto, Lee and Ermann (1999) pointed out car manufacturers *expected* compact cars were not as safe as full-size models. The fire in Hamlet was in no small part due to the demands of consumers for affordable poultry. Considering the crash of the Space Shuttle Challenger, mandates government contracts are given to the lowest bidder may have been created by legislators; but this system has been created to appease taxpayers who do not want their tax dollars wasted. Such circumstances are evident from campaigns by Senator John McCain (R – Arizona) to eliminate government "pork" and from the media via examples such as former news anchor Tom Brokaw doing a regular nightly news special called "The Fleecing of America" which outlined ways the government seemingly wasted taxpayer money.

Corporations and government may cut corners to reap profits or save money, but one of the factors in this rational calculus is the demands of consumers and taxpayers. Consumers want the best products they can obtain for the least amount of money and as a general rule, most people hate paying taxes. In such a climate, problems are natural. State-corporate crime scholars seem to typically be legal paternalists who believe the government should save citizens from both corporations and save citizens from themselves. These scholars seem to believe most people do not have their own best interests in mind and it is not only a government failure when citizens are not

protected, but a crime. This might work for some industries, but prescription drugs provide a unique set of problems.

Although many of the members of Congress and witnesses at the OxyContin® hearings argued the regulatory agencies needed to do more to prevent prescription drug abuse and diversion, most of these witnesses also stated a balancing act was needed. At every hearing there were several medical practitioners testifying patients in pain could not be forgotten and whatever changes made needed to account for these patients. Furthermore, the way many of these witnesses framed the issue, preventing patients from access to prescription drugs might have actually been a greater crime than allowing prescription drugs onto the black market. Such a climate severely limited the amount of options on the table for drug regulators. Many witnesses noted during the 1970s and 1980s, patients did not commonly have access to necessary pain medications. These witnesses stated important changes had been made to allow better pain management.[105] According to these witnesses, although the abuse and diversion of prescription drugs were problematic, legitimate pain patients should not have their medications taken away or severely restricted due to the illegal actions of recreational drug users.

A small number of critics of the pain management movement argued this movement was largely created by pharmaceutical companies.[106] These critics pointed out Purdue Pharma and other manufacturers of pain medication donated large amounts

[105] Dr. Michael Levy (2001a), Dr. Mary Simmonds (2001), Dr. Michael Ashburn (2001), Dr. Richard Payne (2002), Dr. Stacy Berckes (2004), Dr. Karen Kaplan (2004), Dr. Chad Kollas (2004), Dr. Janet Abrahm (2005) and Dr. James Campbell (2007) all stated pain was undertreated, but improvement had been made and it was important not to return to a previous regulatory climate when pain medications were not largely available to pain patients.

[106] Perhaps most forcefully by Marianne Skolek, an LPN who lost her daughter to OxyContin® abuse.

of money and essentially created lobbying groups to change laws and regulatory conditions to create higher profit margins. One witness, Dr. Egilman (2004), stated many physicians were hesitant to prescribe opioids to patients and Purdue Pharma was creating the false perception the medical community was behind the push to make opioids more available. Although Purdue Pharma benefitted from this regulatory climate (until the plea agreement in 2007), the amount of people Purdue Pharma would have essentially had to pay off to make this happen would have been staggering. From the witnesses testifying, it would seem Purdue Pharma had Johns Hopkins University, every cancer center and pain management center in the pockets of the company.

Hawthorne (2005) noted when a pharmaceutical company wanted to speed the drug approval process up, the only thing the company could really do is make telephone calls asking why a delay was occurring. Many are skeptical this really has an effect on FDA decision-making. However, what has proven effective on the speed of FDA decision-making is certain patient support groups. AIDS activists and cancer research activists (especially for breast cancer) have held demonstrations protesting what is perceived as by these groups as inaction on the part of the FDA. Many people represented by these groups are patients that are already gravely ill or dying. If a drug is potentially dangerous to them is immaterial; patients cannot typically have less than no hope. The hope of a cure or possible treatment is worth any risk to these patients. Hawthorne stated, through many interviews she conducted, employees at the FDA were sensitive to the pleas of these patients.

Conclusion

The state-corporate crime paradigm is relatively new. It provides a valuable framework to analyze the actions of the state when regulating the actions of corporations. Whenever this process results in harm, the framework typically dictates these actions were a state-corporate crime. Although this process is instructive, it may often be considered overly simplistic. Since the invention of the hypodermic syringe and the isolation of morphine, the United States has had to deal with the balancing act of allowing patients access to these medications while protecting from abuse and diversion. The drug abuse liability system has often been criticized, but so has every other form of regulation. Whenever an intersection on a road needs a stoplight, many might say an accident must occur before that will happen. In times of limited budgets, money is generally not committed unless a problem needs to be dealt with and governments are rarely proactive. This process is further complicated since few states speak with one voice and rarely is one person given the power to regulate. The American system of government often has to balance multiple interests, many of which are not easily compatible.

The FDA had the power and authority to remove OxyContin® from the pharmaceutical market if the agency had chosen to. The DEA or Congress could have placed OxyContin® into Schedule I if they had chosen to. It would not be the first time or most likely the last time either party has chosen to completely restrict a drug with medical utility. These actions could have occurred, but did not. However, it does not appear that the power or demands of a corporation prevented either remedy, it appears the power and demands of physicians who prescribe and patients who take OxyContin®

were the more compelling voice. It is clear the product caused harm, but denying patients from having the medication most likely would have caused greater harm; in this case by the vast undertreatment of pain. Government agencies seemed to choose pragmatism over being proactive. This resulted in many long overdue changes to the drug abuse liability system. Throughout the entire history of pharmaceutical regulations this has always been the case and it is completely conceivable future change will need another problem drug to serve as the catalyst for additional changes.

From this case study it is clear that corporate crimes occurred. Not only did Purdue Pharma misbrand the drug OxyContin®, but the company also conducted an overly aggressive advertising campaign which promoted a drug that would become highly desirable on the black market into a regulatory climate that was not equipped to handle the new drug. Purdue Pharma should have been well aware this would be problematic, but only chose to take preventive action after it was already abundantly clear OxyContin® abuse and diversion would be problems. However, labeling the second action as “criminal” can be problematic. To Sutherland, such socially injurious behavior would be considered criminal, while Tappan would most likely point out this socially injurious behavior cannot be considered a crime because there is no specific law or offense that prevents this behavior. Certainly, there is no criminal charge for simply taking advantage of a lax regulatory climate. It was never really alleged much less proven that Purdue Pharma was trying to encourage diverted OxyContin® to be abused or diverted. Indeed, many of the actions the corporation took to help prevent abuse and diversion were unprecedented for a pharmaceutical company.

The more difficult question to answer is whether a state-corporate crime occurred. Keeping in mind the existing literature, it seems clear that the state fostered a regulatory climate that was not only inadequate, but known to be so. It seemed only a matter of time until a problem-drug caused harm, which is exactly what happened. However, after this occurred many changes were implemented that not only improved the overall abuse liability system, but have actually been shown to work in the subsequent case of Palladone®. Although it seems clear OxyContin® will not be the last problem drug, one must wonder if there will be another case quite like it. Considering this, perhaps the system worked exactly as it should. Although many had argued the abuse liability assessment system was flawed, few had offered any suggestions of how exactly to fix the system. It simply took a problem drug to expose these problems. Had the proper protections already been in place, most likely OxyContin® and Purdue Pharma would have a very different reputation. Furthermore, some observers argued problems with OxyContin® constituted a moral panic. Although the true amount of harm the drug caused will never be known, perhaps the greatest legacy of the drug will be that it was responsible for so much positive change. Keeping this thought in mind, one might begin to question the notion of a moral panic itself. Were the problems attributed to OxyContin® really about the drug itself or were the problems attributed to OxyContin® actually just a symptom of the larger issue; the deficiencies of the abuse liability system? If this is the case then one can either question the notion of moral panics or illustrate how a moral panic might be useful to initiate positive policy change.

One of the biggest questions of the current study concerns the utility of the state-corporate crime paradigm. Critics of the paradigm can argue, much like Tappan did of Sutherland, the paradigm labels the bad behaviors or inaction of state regulators as criminal actions. This is problematic because not only are inactions (or omissions) not typically criminal actions, supporters of the paradigm seem to want to label what they view as bad policy or bad decisions as criminal actions; even when there is not a corresponding law that prohibits the behavior of the regulators. Perhaps it is not the state-corporate crime paradigm itself that is useful in analyzing the current study, but the approach supporters of state-corporate utilize to conduct case studies. The most useful part of the state-corporate crime paradigm is that it analyzes the structure of the regulatory environment that allows corporations to engage in deviant behavior.

The actions of Purdue Pharma did not happen in a vacuum. These actions occurred at a time when many were pushing for more effective pain management at a time law enforcement agencies were transitioning from simply policing illegal drugs to learning how to deal with the additional problems caused by the abuse and diversion of legal prescription drugs. Additionally, many states did not have prescription monitoring programs which was not only determined by a lack of prioritizing in state budgets, but also from the lack of available technology. The expansion of technology in computing and the internet since 1995 has improved dramatically and the quality of prescription monitoring programs has improved as well. Filling out a prescription form in triplicate only allows law enforcement to apprehend an offender after a crime has been committed; real time information available via the internet can prevent the crime from happening altogether. Perhaps the greatest limitation on government was the choice

the state had to make: were patients in pain who needed medications more important than preventing recreational users of drugs in seeking out and manipulating the most potent opioid yet to reach the market? This essentially caused the state to chose one group of citizens over another; either way one group would be harmed. It seems like no matter what happened harm would occur which ultimately makes the assessment of blame problematic. Perhaps there is no correct answer.

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BIOGRAPHICAL SKETCH

O. Hayden Griffin, III graduated from Blacksburg High School in June of 1994. The following August he matriculated at Virginia Polytechnic Institute & State University. While at Virginia Tech, he served as an associate justice in the Virginia Tech Undergraduate Honor System. He completed a Bachelor of Arts degree in history, as well as a second major certificate in political science in May of 1998. The following summer Hayden served as a Governor's Fellow in the Virginia Governor's Fellows Program. He was assigned to work in the Secretariat of Commerce and Trade while completing the fellowship. In August of 1998, Hayden matriculated at the T.C. Williams School of Law at the University of Richmond. While in law school, Hayden completed a clinical placement in the Richmond City Public Defenders Office. He graduated in May of 2001 with a Juris doctorate. In January of 2004, Hayden began a Masters of Arts degree in political science at Virginia Polytechnic Institute & State University. In January of 2005, he transferred to Radford University and began a Masters of Arts in criminal justice. He completed the degree in August of 2006. His master's thesis was entitled *A Comparative Content Analysis of the Drug Enforcement Administration and Congressional Hearings of MDMA and GHB*. Later that month, Hayden matriculated at the University of Florida and began work toward a Doctorate in Criminology, Law and Society. He was a graduate student teaching assistant for three years and taught eight sections of Criminal Law. In recognition of his work in the classroom, he won the Criminology and Law Honor Society Graduate Student Teaching Award in May of 2009. Hayden's research has been published in the *Critical Criminology: An International Journal*, *Journal of Criminal Justice*, the *Journal of Drug Education*, the *Journal of Psychoactive Drugs* and the *Campbell Law Observer*.