Purdue Pharma Deceptive Research Misconduct

The Importance of the Use of Independent, Transparent, Current Research

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Issue

ABSTRACT

Big Pharma must meet bioethical standards to prevent the misuse of its products and to foster public trust in the greater scientific arena. Independent, transparent research is crucial to the ethical distribution of safe and effective pharmaceuticals. Research must be current and reflect the

population to which it is applied. Competing peer-reviewed published works should be cited in promotional materials so that prescribers and patients can draw informed conclusions and see areas where there is disparate research.

INTRODUCTION

Though "Big Pharma" has a negative connotation to the general public, in many instances this connotation is unwarranted and can hamper pharmaceutical advancement. Through venture capital and financing, pharmaceutical businesses produce new drugs quickly, allowing them to make large profits. However, ulterior financial motives have led certain companies to prioritize transactional values above the health of the consumers, which reflects the companies' disregard for bioethics. This collision of values garners public distrust and negative attitudes toward pharmaceutical companies. For example, Purdue Pharmaceuticals blatantly disregarded standards of bioethics when it propelled its self-proclaimed breakthrough drug, OxyContin®, into the lives of many Americans. The company's success came at an extremely high cost: a death toll in the hundreds of thousands from opiate misuse.[1] Purdue Pharma violated bioethical standards and laws written to protect consumers and the public. This paper will specifically address Purdue Pharma's research methods and their potential biases. It argues that drug research must be current and accurate, use a sample demographic that reflects the target population, and address the potential for misuse of a drug.

ANALYSIS

A. Bioethics Applied to the Business of Medication

Purdue Pharma has developed pharmaceuticals for more than 100 years; over that period, its executives specifically steered the company toward advances in pain management. Although Purdue Pharma is ultimately a business**,** its products can affect the lives of consumers in uniquely dangerous ways. Therefore, the actions of pharmaceutical companies demand the serious consideration of bioethical principles. Arguably, pharmaceutical companies act with beneficence because the medications they produce treat illnesses or alleviate conditions that negatively affect health. OxyContin was originally approved for prescribed use every 12 hours and was heralded as a solution to pain in end-of-life cancer care and other chronic, painful conditions.[2] Yet, drugs for pain management are implicated in the opioid epidemic. To apply the principle of beneficence to their practices, pharmaceutical companies must ensure that the benefits of their drugs outweigh the risks by conducting extensive research into the product's safety and efficacy. Pharmaceutical companies must also minimize risks of the medication that may arise from misuse. In Purdue Pharma's case, it was necessary to perform extensive research into OxyContin's biological effects on its broad target population. However, Purdue Pharma marketed OxyContin as a safe and nonaddictive pain reliever based on only a handful of misrepresented, outdated, and narrow studies. The company used the findings from the cited articles out of context and they did not provide credible evidence.

This ties into the next bioethical principle: nonmaleficence. Purdue Pharma has a bioethical obligation to address the risks of their product even if it is used outside of a clinical setting. Purdue Pharma did not address the risks of addiction to OxyContin and even hid incriminating data, which led to its liberal use by prescribers.[3] Drug developers are not absolved of the responsibility to reduce the potential harm done to the public due to misuse of the drug. OxyContin was among the most abused medications in the opioid epidemic.[4] Not only did Purdue Pharma fail to take responsibility for its part in the opioid epidemic, it also did not take steps to reduce harm.

Nonmaleficence extends beyond harm reduction. Bioethical principles must apply to pharmaceutical companies to ensure public safety and honest business practices. Purdue Pharma pled guilty to fraud and kickback conspiracies, admitting to its role in the opioid epidemic and

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Perspectives

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providing evidence that the company acted in an unprincipled way to profit from people rather than treat them.[5] In excerpts from old studies, Purdue Pharma referred to other opioids created before OxyContin, using the research out of context and inappropriately, and failing to address conflicts of interest. The court ruling that held the company accountable for its role in the opioid epidemic conveys the immorality of its research practices and decisions.

Bioethical principles compel pharmaceutical companies to maintain an ethical landscape that protects consumers and especially vulnerable patients. Maleficent actions and business practices led to a crisis that profoundly impacted society and led to a vast number of people becoming addicted to or dying from opioids. These dismal consequences speak to the need to improve institutional bioethics, to create mechanisms that prevent similar wrongdoing, and to hold companies accountable for their maleficent actions. It is helpful to understand how Purdue Pharma used research inappropriately to institute principled policies.

B. Overgeneralization, Fraud, and Conflict of Interest in Citing Research Studies

While Purdue Pharma marketed OxyContin through brochures, the marketing literature asserted it had a low or nonexistent risk of addiction. Purdue Pharma's emails to doctors argued for higher doses of OxyContin.[6] The company cited research studies and a paragraph-long publication in the *New England Journal of Medicine* to justify its claims about the safety and efficacy of higher dosages of OxyContin. In 1980, Hershel Jick and Jane Porter contributed a one paragraph letter to the editor in *The New England Journal of Medicine* expressing that they found an extremely low rate of addiction in closely monitored hospitalized patients.[7] Purdue Pharma used this paragraph to add credibility to their claims that OxyContin is highly unlikely to be an addictive substance. This article from 1980, which was not accompanied by any research, had been cited 608 times by 2017, mostly to support the contention that opioids were not addictive.[8] Purdue Pharma grossly misrepresented the findings indicated by Jick and Porter in several ways. First, Jick and Porter's article is not a research article as it has no empirical data, methodology, or discussion about the conducted study. The company should not have used it as evidence to support its claims. Additionally, Jick's letter was published 15 years before OxyContin's FDA approval but was cited three years after its approval in the brochure.[9] Purdue Pharma should have cited more recent data. In some brochures, Purdue Pharma did not disclose the study demographic as hospitalized inpatient individuals and claimed that in a "survey of more than 11,000 opioid-using patients, taken over the course of several years, [they] found only four cases of documented addiction."[10] Jick and Porter concluded that hospitalized patients without history of addiction only had a low risk of addiction when exposed to low doses of narcotics. These patients were not offered opioids for home use and the study did not follow the patients post-discharge. The findings should not have been generalized outside the study demographic.

The fact that the drug was studied in the hospital setting is crucial. There is a difference between someone who cannot leave the hospital due their medical condition and someone who can willingly go to a doctor's office to ask for a prescription. In the hospital setting, there are methods to strictly control the dispensing of medications, unlike in certain circumstances where use is not monitored.[11] Purdue neglected to address the differences between hospitalized patients and the general public. OxyContin was marketed for inpatients and outpatients based partly on this survey study that considered only the inpatient population.

Purdue Pharma regularly cited a questionnaire-based study, written by Samuel Perry and George Heidrich and published in 1982, that reported analgesic methods used during debridement of wounds in burn facilities throughout the United States.[12] Arguably, the study was not misinterpreted, and its findings do apply to a portion of OxyContin's intended demographic. Yet, the study should not be generalized beyond hospitalized burn patients as their use of the drug was both monitored in a controlled environment and used for a specific painful condition. The study does not justify the use of OxyContin in acute, non-cancer related pain. However, makers of OxyContin claimed that the drug could treat a wide variety of pain syndromes, from mild lower back

pain to severe acute trauma. Purdue Pharma cannot rely on research derived from hospitalized burn patients to justify the use of OxyContin in multiple conditions. To make broad claims, a more representative pool of subjects is required.

Purdue Pharma's use of the Perry and Heidrich study should be strictly scrutinized. The respondents to the questionnaire were nurses, clinicians, and physicians who assessed the pain of hospitalized burn patients. Medical professionals can succumb to biases like everyone else. They may have felt compelled to uphold the reputation of their facility by indicating no incidence of addiction. Addiction has long been stigmatized; when the study was conducted, the popular paradigm was that addiction could be attributed to a person's lifestyle. Only recently has addiction been seen as an illness rather than a lifestyle choice. While there may have been confounding factors that influenced the results of the questionnaires, there is no indication that there had been any follow-up investigation with the respondents.

According to *The People of the State of California v. Purdue Pharma,* Purdue Pharma funded research to investigate the addictiveness of OxyContin. Lawrence Robbins, who led the research, found that "8 % of the patients who took OxyContin to treat concurrent migraines displayed enough addictive behavior to qualify for prescription abuse."[13] In another study from 1998, Robbins observed addictive behavior in 13 percent of patients taking OxyContin for chronic daily headache.[14] Instead of relying on the Robbins study, Purdue Pharma used the Perry and Heidrich study to push their narrative of a nonaddictive drug. The Perry and Heidrich study fails to provide empirical data, methodology, or procedures from individual facilities. In addition, the study did not provide records from the hospitalized burn patients and did not address post-hospitalization opioid use. This study is a poor choice as evidence of OxyContin's nonaddictive properties.

When referring to studies in its brochures, the company paraphrased and made unsupported claims. Gary Franklin, a physician and professor at the University of Washington, wrote *Interagency Guideline on Opioid Dosing for Chronic Non-Cancer Pain* for the state of Washington, which recommended strict restrictions and dosages for opioid use.[15] In response to Washington's guidelines, Purdue Pharma argued for higher dosages and claimed that opioids were safe. They claimed that the classification of OxyContin was faulty.[16] In an email sent to Franklin to influence the policy, the company referred to studies that were either partially or fully funded by Purdue Pharma. Notably, one study was conducted by employees of the company.[17] Arguably, if pharmaceutical companies are ethically bound to ensure product safety, they are also obligated to fund research into those drugs. During the process of product development, the company does the research. However, financial incentives can create a conflict of interest that may sway the researchers or the company's use of the research. Company researchers may feel obligated to produce results that would benefit Purdue Pharma, also creating a conflict of interest. A literature review of financial conflicts of interest in biomedical research "showed a statistically significant association between industry sponsorship and pro-industry conclusions."[18] Purdue Pharma was deceitful and should have used independent research.

As a result of the studies by Robbins, the company knew OxyContin's addictive potential and yet did not disclose the findings in their communications. Years later, Jick stated in an NPR podcast that he regretted writing that old one-paragraph piece with Porter in the *New England Journal of Medicine*. Jick commented on the unexpected result, admitting, "it was used by drug companies who created these…these new opioids and concluded that they were not addictive…but that's not in any shape or form what we suggested…in our letter."[19]

CONCLUSION

While Purdue Pharma is bound by bioethical principles, its actions left a lasting scar on the pharmaceutical industry, medical community, and the nation. Several practices contributed to mistrust of Big Pharma and the broader scientific community: committing acts of fraud and deceit, ineffectually generalizing research to people outside of study demographics, and using outdated,

biased research. Purdue Pharma, which made more than 35 billion dollars selling OxyContin, later pled guilty to felony wrongdoing and reached a settlement of 8.3 billion. The company may be repurposed as a public benefit company.[20] While the Purdue Pharma story is haunting, a few lessons should not be overlooked. The quality of safety research matters. Independent, transparent research is crucial to the ethical distribution of safe and effective pharmaceuticals. Research must be current and reflect the population to which it is applied. Competing peer-reviewed published works should be cited in promotional materials so that prescribers and patients can draw informed conclusions and see areas where there is disparate research. Big Pharma must meet bioethical standards to prevent the misuse of its products and to foster public trust in the greater scientific arena.

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