Scientific misconduct in the pharmaceutical industry

Marie-Louise Hoogendoorn and Anouk de Lange

Interdisciplinary Social Sciences and Sociology

Abstract
In the area of pharmaceutical research, misconduct has become a well-known phenomenon that has many different determinants. Developing a drug costs pharmaceutical companies a lot of money. The investing industries and academic institutions seem to have a financial conflict of interest. For example, when researchers and the media eventually discovered that some patients who took Prozac experience serious side effects (even suicide) the drug was already popular and doctors continued to write prescriptions. This is an issue that should be taken seriously because this involves human lives.

Keywords: pharmaceutical companies, Prozac, pharmaceutical misconduct, drug costs, financial conflict of interest.

Introduction

Scientists have generally been seen by the public at large as objective truth seekers. Fanelli (2009) argues that this traditional image of scientists seems to be jeopardized by the recent revelations of several high-profile scientific fraud cases. Hwang Woo-Suk with his fake stem-cell lines and Jan Hendrik Schön with his outlandish claims and duplicated graphs, are but two recent examples of academic cheating (Fanelli, 2009). Unfortunately, misconduct among researchers appears to be on the rise (Kornfeld, 2012). There not only seems to be a growing number of fraud cases. Research also shows that those cases of fraud that are actually discovered represent no more than the tip of the iceberg (Fanelli, 2009).

But what constitutes scientific misconduct? Fanelli (2009) argues that fabrication (invention of data or cases), falsification (distortion of data or results) and plagiarism (copying of ideas, data or words without attribution) are forms of scientific misconduct. These various forms of misconduct have the potential to harm science (Kornfeld, 2012). Fanelli (2012) conducted the first meta-analysis of surveys asking scientists about their experiences with scientific misconduct: 1.97% of the scientists admitted having fabricated or falsified data results at least once, and 33.7% reported having engaged in other questionable practices. There was also a question about the behavior of colleagues: 14.12% reported that they knew of cases in which colleagues falsified data and 72% reported suspecting questionable practices on the part of their peers. The study also shows that there was more misconduct reported by medical and pharmaceutical researchers than by other scientific researchers.

The Dutch scientific community was recently shaken by revelations that two well-known scientists had been falsifying and fabricating data (van der Wal, 2012). These kinds of events raise an important question: Why would an intelligent and ambitious professional risk everything by committing fraud? There are several factors that could result in scientific misconduct, including the high pressure on scientists to publish their research. For a scientist, it is important to receive a subsidy or contract to be able to continue doing research (Komter, , 2012). The growing number of talented scientists, along with recent improvements in

scientific technology, mean that there is potential to achieve significant advances in knowledge. On the other hand, the funds that support research are insufficient. This results in a competitive scientific environment in which people have to publish in order to survive and thrive (Kornfeld, 2012).

As mentioned before, scientific misconduct is now a well-documented phenomenon with multiple determinants. In recent years, the pharmaceutical industry has progressively increased its sponsorship of medical research (Woolley, 2011).

Fanelli (2009) argues that strong feelings of competition exist among researchers in the pharmaceutical industry, which is fundamentally driven by the need to make profit. In terms of scientific research, they have an interest in positive outcomes. Studies have shown that some pharmaceutical companies are indeed guilty of promoting academic cheating in order to expand markets (Kitsis 2009). This raises the question: In what way does the pharmaceutical industry influence scientific misconduct? Is there any evidence to be found that answers the main question of this article: How does the pharmaceutical industry influence scientific misconduct?

Through this literature review, we have searched for cases in which pharmaceutical research (especially regarding the anti-depressant drug Prozac) was questioned.

Historical perspective

The 21st century offers the potential for significant advances in medical research. The public now has generally high expectations of medical research and its possible lifesaving discoveries. However Cohen (2005) argues that news about financial conflicts of interest and recent high-profile cases of scientific misconduct threaten to undermine public trust in academic institutions. The present era faces more daunting challenges of medical research than previous generations. Cohen (2005) argues that creating high expectations of medical breakthroughs is an effective way of getting public support for funding medical research. The partnership of pharmaceutical industries and academic institutions has grown in the past decades, and the former must use the latter's expertise to develop useful medicine and services (Cohen, 2005). But nowadays, there seems to be a financial conflict of interest. Pharmaceutical companies want to create and sell as many products as possible and therefore have the potential to undermine the integrity of scientific studies, which in turn can lead to public distrust of the enterprise of pharmaceutical research (Cohen, 2005).

In response to the discovery of several fraud cases in recent years, governments have increasingly felt obliged to intervene in order to prevent and sanction scientific misconduct (Golner, 1988). As far back as in 1980 various academic institutions (including Harvard Medical School) and national agencies began drafting strict guidelines to increase public awareness of the standards of honest scientific behavior, and to promote good science (Shore, 1995). The discovery of recent pharmaceutical fraud cases shows that the phenomenon of scientific misconduct still exists, even after recent institutional and governmental interventions (Kitsis, 2009).

Academic institutions that conduct medical research face many challenges in the future. Cohen (2005) contends that these institutions can benefit from the growing relationships with the pharmaceutical industry only when they remain true to fundamental academic values. Pharmaceutical companies will always have an interest in positive outcomes and selling their products. Brownlee (2004) raises the question as to the appropriateness of medical researchers who have a financial stake in products (medication) being allowed to conduct scientific research involving those

products. Studies of the history of research show us that, especially during the past two decades, medical research has become corrupted by cash from the pharmaceutical industry.

Another point of view is that, according to Lindblad (2002), the 20th century was characterized (especially during its last two decades) by heightened awareness and extensive dialogue regarding the problem of scientific misconduct, a phenomenon that has always existed, in medical research and elsewhere, have always existed. Cohen (2005) emphasizes the importance of ethical research within medical science in terms of 'doing no harm' to human lives.

Fraud in pharmaceutical research

As stated previously, scientific knowledge has become very important in 21st century societies. It is used as a basis for public policy decisions, to learn more about the world we live in, and to improve human life. Science has been especially successful in this last task, and this is one of the reasons people live a lot longer now than they did just one-hundred years ago. But discovering drugs that work, or improving those already on the market, requires a lot of research and testing. Science is the perfect tool for determining whether there is a relationship between two factors or variables. These factors can of course be manipulated. The important question here, in the context of pharmaceutical research, is the extent to which such manipulation violates accepted ethical standards manipulation necessary, ethic or, in the pharmaceutics industry, healthy and not dangerous (Avery, 2010). This kind of misconduct is sometimes perpetrated by researchers who hold stock in companies who sell these drugs. Pharmaceutical companies finance these researchers and exploit their credibility in their marketing.

The main goal for any business is, of course, to sell its products. This is no different for pharmaceutical companies. But in this case, if the product doesn't work, it can claim human lives. So it is important that research be done professionally, and that any advertising in connection with pharmaceutical products be within ethical boundaries. But research is not always done professionally. To sell their products or to promote them, these companies often finance or conduct their own research with a heavy confirmation bias. There are a lot of companies who do honestly conduct their own research (and/or are forced to do so because they cannot secure funding to have research conducted by an independent entity). However, sponsorship of research by pharmaceutical companies with a vested interest in said research has often led to manipulation of data or suppression of adverse results in order to support government approval of new products or drugs (Avery, 2010). A number of studies have been conducted on the conflict of interest that may arise in such situations.

Lexchin, Bero, Djulbegovic, and Clark (2003) conducted a study that explored how pharmaceutical research is done. Their conclusion was that the pharmaceutical industry in the United States now spends more on medical research than the National Institutes of Health. Most research is done by the company itself or externally by researchers who get paid by the company, because of the financial risks that bad outcomes can have for the pharmaceutical company.

More than 25 years ago, Richard A. Davidson (1986) found a statistically significant association between the source of funding and the outcome of the research. A total of 107 research studies were examined, all conducted by pharmaceutical companies or researchers sponsored by these companies. A total of 29 percent of these trials favored traditional treatment, while 71 percent favored treatment involving the new drug being evaluated.

The bias involved in such a phenomenon does not only influence the general public, but also medical journals.

When such a journal publishes an article reporting positive results about a particular drug, it lends the article in question its scientific prestige, and thus inspires the confidence of both the scientific community and the general public (Portela Camara, 2006).

We can conclude, on the basis of such research outcomes, and keeping in mind that these companies have to sell their products, that it is highly likely that these companies will make sure that whatever outcomes are obtained will place their product in a favorable light. That means that there is a kind of invisible pressure laying on the pharmaceutical research, because they have come up with new medication and for them it needs to be successful.

Prozac

Positive outcomes seem to have been assured in research conducted on Prozac, an anti-depressant medication introduced in 1988. Its prescribing information identifies Prozac as a 'selective serotonin reuptake inhibitor for oral administration'. Prozac is indicated as a possible treatment of different mental disorders, for example for major depressive disorder, obsessive-compulsive disorder, panic disorder or bulimia nervosa and binge eating disorder. Compared to other antidepressants, Prozac has fewer serious side effects. Because treatments for depressive disorders have been highly variable in their effectiveness, were highly intrusive, or involved serious side effects, Prozac quickly received widespread acceptance among physicians and the general public following the initial reports of its effectiveness (Marshall, 2007). During Prozac's first year on the market, prescriptions for more than 2.4 million individual patients were written. That is important evidence for the medicalIn 1995 sales exceed one billion dollars and, by2002, it had been prescribed 33 million times. It was advertised as a drug with minimum side effects. But, during the 1990s, Prozac's side effects began to be widely debated in the media. There even is research that proves that a possible side effect of Prozac is be death by overdose (Marshall, 2007).

Nevertheless, Eli Lilly and Company, which developed Prozac, continued to invest big money in advertising Prozac, without making any statements about possible side effects. An example of the wide public acceptance of Prozac could be seen in a 1990 cover article in Newsweek headlined: "Prozac: a breakthrough drug for depression". In 1997, in part due to 'cultural lag'[1], critics began to increasingly question the safety of the drug. This was not only because of the evidence suggesting a possible link with suicide, but also because of the increasing self-destructive behavior of people taking Prozac. There were many reports written about the medication's negative effects, but these were largely ignored by the general public, and physicians continued to write prescriptions for Prozac on a massive scale. By this time, there were also more and more people claiming that Eli Lilly had deliberately concealed information regarding the risks of Prozac, even during the FDA approval process.

Or, to take a different viewpoint, one could ask whether Prozac is perhaps just good business and if it is instead the frequency of depressive disorder that is exaggerated. In their book, 'The loss of sadness: how psychiatry transformed normal sorrow into depressive disorder', Horwitz and Wakefield (2007) argue that the current criteria for depressive disorder are not very different from the normal sadness all people will experience at some point in their lives. They contend that this has led to grossly inflated numbers of persons being diagnosed with depressive disorder. In their view, it was the tendency of physicians to overdiagnose depression

[1] According to sociology.about.com, 'cultural lag' is a term used to describe what happens in a social system when the cultural ideas used to regulate social life do not keep pace with other social changes.

in patients that led to an estimate of 100.000 per million people being diagnosed with a depressive disorder at the beginning of the 21st century. In the 1950s, this number was a mere fifty people per million (Healy, 2000). As with other disorders, the list of symptoms that is stated in the Diagnostic and Statistical Manual of Mental Disorders (DSM) has been highly improved over time, but also expanded. The predictable result is that that there is not only improved treatment of these disorders, but also more patients being diagnosed with depressive disorders. This leads to the following question: Does everybody who gets a prescription for Prozac or some other anti-depressant really suffer from a major depressive disorder, or are many of them just temporarily sad?

Developing a new drug requires a big investment on a number of fronts. There is obviously a lot of money needed, human resources, technological expertise and a lot of time and patience. There are also strict regulations about testing and, as previously noted, there is an FDA approval process that needs to be completed before the drug can be prescribed to the general public.

So what happened during the process that began with the development of Prozac, and that concluded with the discovery of its potentially lethal side effects? There is no single answer to that question. But what we can say with a high degree of certainty that Eli Lilly did not appear to always be playing by the rules, and that it may have been overly eager to aggressively market a drug for depressive disorders. One might also say that Eli Lilly simply did a great job in marketing Prozac. We can also credit the media, the public and maybe even the DSM for Prozac being such a smash success since the first day it is on the market.

Conclusion and discussion

We can conclude that, despite widespread disapproval of the practice, many medical scientists continue to knowingly allow their research to be influenced. There are different kinds of scientific misconduct. There are more and more discoveries of researchers who are guilty of fabrication, falsification and plagiarism. One area where misconduct has been very widely discussed is in the pharmaceutical industry. This is because misconduct in that industry can end up seriously damaging - or even ending - human lives. But one finds, in evaluating studies of pharmaceutical research, that scientific misconduct is almost a logical consequence of prevailing conditions. Most pharmaceutical companies don't secure sufficient money from the government and other funding sources, and they are therefore forced to either sponsor or conduct research of their own products. The predictable result of this process is often that outcomes favor of the companies' product. What happened in the case of Prozac illustrates this phenomenon clearly. The company that produced Prozac, Eli Lilly and Company, did the research itself. They then conducted a massive campaign to market the drug, and Prozac became quickly very popular. By the time serious side effects (including suicide) in association with use of the drug began to be reported, it already was so popular that patients continued to demand, and doctors continued to prescribe, the medication. Eli Lilly, after initially refusing altogether to address harmful side effects, began to do so only after a significant amount of damage had already been done. Another reason for the popularity of Prozac is the increasing popularity of the DSM in psychiatric and medical circles. Specifically, the fact that successive versions of the DSM list more and more depressive symptoms has led more and more physicians to diagnose their patients as suffering from a major depressive disorder.

Our emphasis throughout this paper has been on the negative practices of the pharmaceutical industry. We looked more at the negative reviews about Prozac, even though there are plenty of people who are

really helped by using it. So while the industry should not go without public and scientific scrutiny, we should not disregard the positive effects of pharmaceutical innovations and the health benefits that they bring. In fact, as we previously mentioned, it is possible that media criticism of pharmaceutical companies might lead to an overemphasis of controversies and misconduct, and to a negative bias toward such companies that may be unjustified, but a fact is that there is a lot going on in the pharmaceutics people are not aware of.

References

Avery, G. (2010). Scientific misconduct: The perversion of scientific evidence for policy advocacy. *World Medical and Health Policy,* 2(4), Article 3.

Davidson, R.A. (1986). Source of funding and outcome of clinical trials. *Journal of General Internal Medicine*, 1(3), 155-158.

Fanelli, D. (2009). How many scientists fabricate and falsify research. A systematic review and meta-mnalysis of survey data. *PloS One*, 4(5).

Goldner, J.A. (1998). The unending saga of legal controls over scientific misconduct: A clash of cultures needing resolution. *American Journal of Law and Medicine*, 24(2-3).

Healy, D. (2000). Good science or good business? *Hastings Center Report* 30(2), 19-22.

Horwitz, A.V. & Wakefield, J.C. (2007). *The loss of sadness: How psychiatry transformed normal sorrow into depressive disorder*. Oxford University Press: New York.

Kitsis, E.A.(2009) . Rx for the pharmaceutical industry: Call your doctors. *Hastings Center Report*, 39(4), 18-21.

Lexchin, J., A Bero, L., Djulbegovic, B. & Clark, O. (2003). Pharmaceutical industry sponsorship and research outcome and quality: systematic review. *British Medical Journal*, 326(7400), doi: 10.1136/bmj.326.7400.1167

Marshall, K., Georgievskava, Z. & Georgievsky, I. (2007). A cultural lag perspective of new drug diffusion and adoption: the case of Prozac. *Proceedings of the Annual Meeting of the Association of Collegiate Maerketing Educators*, pp. 72-75.

Portela Camara, F. (2006). Ethics and conflicts of interest in psychiatric research. *Revista Latinoamericana de Psicopatologia Fundamental*, 9(2), 195-202.