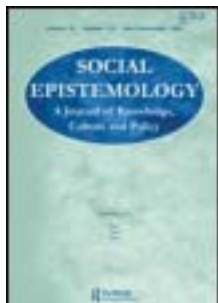


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Lessons from the Vioxx Debacle: What the Privatization of Science Can Teach Us About Social Epistemology

Justin Biddle

Since the early 1980s, private, for-profit corporations have become increasingly involved in all aspects of scientific research, especially of biomedical research. In this essay, I argue that there are dangerous epistemic consequences of this trend, which should be more thoroughly examined by social epistemologists. In support of this claim, I discuss a recent episode of pharmaceutical research involving the painkiller Vioxx. I argue that the research on Vioxx was epistemically problematic and that the primary cause of these inadequacies was faulty institutional arrangements. More specifically, the research was organized in such a way as to allow short-term commercial interests to compromise epistemic integrity. Thus, the Vioxx case study, in conjunction with numerous case studies developed elsewhere, provides strong reasons for believing that the privatization of the biomedical sciences is epistemically worrisome, and it suggests that the primary response to this situation should be a social, or organizational, one. What kind of organizational response would be most beneficial? I briefly discuss two prominent social epistemological proposals for how scientific research should be organized—namely those of Philip Kitcher and Helen Longino—and I suggest that they are incapable of dealing with the phenomenon of privatization. I then draw upon the Vioxx episode in order to outline an alternative suggestion for reorganizing certain aspects of pharmaceutical research.

Keywords: *Vioxx; Social Epistemology; Privatization of Science; Commercialization of Science; Longino; Kitcher*

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The last quarter-century has witnessed dramatic changes in the organization of scientific research. While the period in the USA between the end of WWII and the early 1980s saw patterns of organization in which scientific research was funded primarily by the federal government, the last 25 years have witnessed dramatic shifts in these patterns. The funding of science has been shifting steadily away from the federal government and toward private, for-profit corporations. As a result, both universities and governmental regulatory agencies are becoming increasingly dependent upon corporate financing (Krimsky 2003; Mirowski and Sent 2002).

Some defend the shift toward privatization, arguing that greater involvement by private companies will facilitate the transfer of knowledge from university settings into the marketplace; this, they argue, will result in benefits not only for businesses but for consumers as well.¹ No doubt, such benefits have sometimes occurred. However, a growing amount of research is showing that the ongoing privatization of science, especially in the biomedical sciences, is presenting serious epistemic and ethical costs.² According to this research, privatization is affecting not only the choices of problems to pursue; it is also degrading the quality of research. For example, quantitative studies of articles that evaluate pharmaceuticals are establishing the existence of a “funding effect”; research that is funded by for-profit corporations tends to come to conclusions that are in the interests of those companies (e.g. Bekelman, Li, and Gross 2003; Stelfox et al. 1998). This does not, in itself, establish that the source of funding is causally related to research outcomes; perhaps private, for-profit companies only undertake studies when they have very strong reasons for believing that the results will come out in their favor (Bok 2003). Yet, when these quantitative studies are viewed in conjunction with other works that examine the ways in which many for-profit entities conduct their research, the case that such research is epistemically problematic becomes increasingly clear (e.g. Angell 2004; Avorn 2004; Krimsky 2003). Given this, it is ever more important—both epistemically and ethically—that we evaluate the phenomenon of privatization and find ways to improve the ways in which research is organized.

This paper is a discussion of how social epistemologists should respond to the privatization of the biomedical sciences. More specifically, I hope to accomplish two aims. The first is to show that the privatization of the biomedical sciences, and of science more generally, should be an important item on the agenda of social epistemologists. I will do this by discussing a recent case of pharmaceutical research, namely the Vioxx episode. I will argue that the research on Vioxx was epistemically problematic and that the primary cause of these inadequacies was faulty institutional arrangements. The Vioxx case study, thus, provides further reasons for believing that the privatization of the biomedical sciences is presenting serious epistemic costs, and it suggests that the primary response to this situation should be a *social*, or organizational, one.

This leads to the second aim of the paper, which is to begin to discuss which kinds of social, or organizational, responses would be most beneficial. I will discuss briefly two prominent social epistemological proposals for how scientific research should be organized—namely those of Philip Kitcher (2001) and Helen Longino (1990, 2002a)—and I will suggest that they are incapable of dealing with the phenomenon of privatization. I will then draw upon the Vioxx episode in order to develop a different proposal.

The Vioxx case study provides a helpful illustration of the kinds of considerations that must be taken into account by an adequate proposal for organizing research. More specifically, it suggests that an adequate proposal should acknowledge the fact that, in many areas of science, large power differentials play a significant role in the research process. Drawing upon this insight, I present the outlines of a proposal for reorganizing certain aspects of pharmaceutical research.

The structure of this paper, then, is as follows. In Section I, I examine briefly the proposals by Kitcher and Longino for how scientific research should be organized. In this section, I discuss some preliminary reasons for believing their accounts to be inadequate. Sections II–V are a discussion of the Vioxx episode. In Section VI, I return to the proposals of Kitcher and Longino, and I present an alternative proposal that takes into account the lessons of the Vioxx case.

I. Social Epistemology and the Privatization of Science

Philosophers of science have largely ignored the ongoing privatization of science.³ A few of them, however, have attempted to articulate how scientific research, in very broad terms, should be organized. Kitcher, for example, has articulated his ideal of “well-ordered science,” an ideal form of organization that would purportedly ensure that research is both epistemically reliable and democratically responsive (Kitcher 2001).⁴ According to this proposal, ideal deliberators, who are somehow representative of the public, are tutored in various respects by disinterested, ideal experts; these deliberators, on the basis of their discussions with one another and with their disinterested technical advisors, determine answers to such questions as to which research projects to pursue, and how research should be applied. Similarly, Longino has attempted to characterize an ideal scientific community, one that would ensure that research is both morally and epistemically acceptable (Longino 1990, 2002a). An ideal community, in her view, possesses the following four characteristics: public venues for the criticism of research, uptake of criticism, shared standards for the evaluation of research, and a tempered equality of intellectual authority.

The proposals of Kitcher and Longino face a number of different problems, both theoretical and practical in nature. These problems constitute strong reasons for believing that neither proposal is adequate to help us solve the problems resulting from the privatization of science. In the interests of space, I must simply refer the reader elsewhere for extended discussions of these problems.⁵ In order to motivate the discussion of the Vioxx episode, however, it will be necessary to mention two difficulties that both proposals face. Following the discussion of the Vioxx case, I will return briefly to these proposals in order to present one further problem with them.

The first problem with the proposals of both Kitcher and Longino is their overly general character. Both philosophers attempt to articulate purely general accounts of the organization of research—that is, accounts that apply to all areas of scientific research. Yet, there is little reason to believe that a completely general account can be successful. Different scientific communities in different areas of science face very different issues, and there is no reason to believe that the epistemic issues facing, say,

pharmaceutical researchers and mathematical physicists working in quantum field theory should be met with the same organizational remedies. *Perhaps* they should, but this should not be assumed from the outset. Just as philosophers of science, since Arthur Fine's 1988 Presidential Address to the Philosophy of Science Association, have gone "back to the laboratory" and begun to give up the quest for purely general explications of fundamental methodological concepts (Fine 1988), so should social epistemologists focus upon specific areas of science and attempt to determine, on a case by case basis, how these particular areas should be structured.

The second problem is their overly abstract character. Both of these philosophers intend for their ideals to be relevant to actual scientific communities—Kitcher, for example, has written that the "philosophy of science should earn its way by trying to draw specific morals for the organization of scientific research" (1993, 305). Yet, neither of their proposals is informed in any serious way by discussions of the *actual* organization of research. Kitcher draws upon the tools of microeconomics and Bayesian decision theory, and both Kitcher and Longino draw upon their intuitions about knowledge, justification, and the epistemic significance of rational deliberation; neither, however, draws significantly upon concrete discussions of the ways in which scientific communities are actually organized. If philosophers of science are to provide helpful advice regarding the organization of research, then their proposals should be well-informed by examinations of how science is actually structured.

Instead of proposing purely general, ideal forms of organization that are divorced from the complexities of actual science, I suggest that social epistemologists attempt to make organizational recommendations on the basis of richly textured discussions of the ways in which specific scientific communities are actually organized. In the remainder of the paper, I begin to do this through an examination of the research on the pharmaceutical, Vioxx. This case study represents a helpful basis upon which to make proposals for how pharmaceutical research should be structured; by identifying the ways in which certain organizational arrangements contributed to epistemic inadequacies, we can gain insight into how pharmaceutical research should be reorganized. It is to this case study that I will now turn.

II. The Rise and Fall of Vioxx: A Brief Overview

Rofecoxib, or Vioxx, is a painkiller that is in a class of drugs known as cyclooxygenase-2 (COX-2) selective non-steroidal anti-inflammatory drugs (NSAIDs). Owned by Merck & Co., Vioxx was prescribed for the treatment of arthritis and, in general, for the alleviation of pain. COX-2 inhibitors were developed in the hope that they would be an improvement over traditional (nonselective) NSAIDs, a group that includes aspirin, ibuprofen (Motrin), and naproxen (Aleve). Non-selective NSAIDs block two enzymes: COX-1 and COX-2. Blocking COX-1 has a number of potential consequences, including preventing blood clots that could lead to heart attacks or strokes and damaging the stomach and the intestines. Because of the latter effect, some patients taking NSAIDs are at risk of developing serious ulcers. COX-2 inhibitors, by contrast, block COX-2

but not COX-1; it was hoped that they would alleviate pain to the same degree as traditional NSAIDs with reduced gastrointestinal toxicity.

Merck applied for approval of Vioxx from the US Food and Drug Administration (FDA) in November 1998 and received approval in May 1999. In January of 1999, a large study called the Vioxx Gastrointestinal Outcomes Research (VIGOR) was begun (Bombardier et al. 2000). The results were published in November 2000 in the *New England Journal of Medicine*. The paper had 13 principle authors; two were full-time employees of Merck, and the rest had financial ties to the company (Bombardier et al. 2000, 1527). In the study, approximately 4000 patients who suffered from rheumatoid arthritis were given 50 mg of Vioxx daily (twice the FDA approved amount for long-term usage), and approximately 4000 were given 500 mg of naproxen daily. The goal of the study was to compare the number of gastrointestinal events that occurred in the two groups. The researchers found that Vioxx and naproxen were similarly efficacious in alleviating pain and that Vioxx was associated with significantly fewer gastrointestinal events.

Yet this was not the only result of the study. It also found that the incidence of myocardial infarction (heart attacks) was four times greater in the Vioxx group than in the naproxen group (0.4% to 0.1%) (Bombardier et al. 2000, 1520). While the authors of the study do not provide a definitive explanation for this difference, they suggest that the difference is due to the ability of naproxen to *reduce* the risk of heart attack and not to a tendency of Vioxx to increase it. Vioxx, they suggested, doesn't cause heart attacks; it simply doesn't protect against them.

Given that the results of the VIGOR study raised the possibility that Vioxx contributes to cardiovascular problems, many believed that, at this point, Merck should have investigated this possibility directly. In May 2000, executives at Merck met to discuss precisely this question (Berenson et al. 2004). Yet, after input from both company scientists and marketing officials, Merck decided against performing additional studies to test the cardiovascular effects of Vioxx. While Merck denies that this decision was driven by marketing concerns, marketing officials at the meeting were strongly opposed to this option. The *New York Times* quotes a slide from a presentation at that meeting as reading: "At present, there is no compelling marketing need for such a study. Data would not be available during the critical period. The implied message is not favorable" (Berenson et al. 2004, online article). In other words, performing a study that directly investigated the question of whether Vioxx contributes to cardiovascular problems would have sent the wrong signal—"wrong" with respect to the marketing concerns of the company.

Meanwhile, scientists outside of Merck were becoming increasingly concerned with the reliability of Merck's claims regarding the cardiovascular safety of Vioxx. For example, in August 2001, Mukherjee, Nissen, and Topol published an essay in the *Journal of the American Medical Association* entitled, "Risk of Cardiovascular Events Associated with Selective COX-2 Inhibitors." This study reviewed the results of the two major studies involving two different COX-2 inhibitors—the VIGOR study and the CLASS study, which examined Pfizer's Celebrex—as well as two smaller trials. The study concluded that there was a statistically significant difference in the number of

cardiovascular events between Vioxx and naproxen in the VIGOR trial, while there was no such difference between Celebrex and other non-selective NSAIDs (either ibuprofen or diclofenac). Another relevant study, led by Wayne A. Ray and published in January 2002, was entitled “Non-Steroidal Anti-Inflammatory Drugs and Risk of Serious Coronary Heart Disease: An Observational Cohort Study” (Ray et al. 2002). His group reviewed data from the Tennessee Medicaid program and found that the cardioprotective effects of naproxen are not sufficient to account for the differences in observed cardiovascular problems in the VIGOR trial. On August 11, 2002, partly on the basis of criticisms such as these, the FDA required Merck to add a stronger warning label on Vioxx, which included mention of cardiovascular risks (Topol 2004).

Unpersuaded by its critics, Merck continued to assert the safety of its product. For example, on May 22, 2001, Merck published a press release entitled “Merck Confirms Favorable Cardiovascular Safety Profile of Vioxx.” In this release, Merck denied that Vioxx increased the risk of cardiovascular problems; it asserted that studies have shown that there is “no difference in the incidence of cardiovascular events” between Vioxx and placebo or between Vioxx and other painkillers.⁶ Which studies ostensibly show this is unclear. It might be that the study to which they were referring was a Merck sponsored study published in November 2001 in the journal *Circulation*. This study has seven authors; five were full-time employees of Merck, while the other two were paid consultants to Merck (Konstam et al. 2001, 2280). Like the studies performed by Mukherjee et al. and Ray et al., it was an analysis of patient records that attempted to compare those treated with Vioxx against those treated with placebo or with non-selective NSAIDs. Its conclusion was that there was no difference in cardiovascular events between the three groups.

Merck’s confidence in the safety of Vioxx, however, did not last. On September 30, 2004, Merck pulled Vioxx from the market for causing precisely the cardiovascular problems that the company had earlier denied. The study that eventually led to the withdrawal of Vioxx, the Adenomatous Polyp Prevention on Vioxx (APPROVe), was a Merck-sponsored clinical trial, begun in early 2000, to test whether Vioxx could prevent colon polyps, which can become cancerous (Berenson et al. 2004). This study was a prospective, randomized, double-blind trial that included approximately 2600 patients; individuals with cardiovascular disease were, as in the VIGOR trial, specifically excluded. The trial was supposed to last almost three years, but it was stopped by the monitoring board after 18 months. Of the patients in the Vioxx group, 3.5% suffered a heart attack or stroke, as compared to 1.9% of patients in the placebo group.

The firestorm that the Vioxx withdrawal has caused—in medicine, in business, and in the popular media—has been immense. The FDA has estimated that as many as 55 000 people might have died as a result of taking Vioxx (Harris 2005). Thousands of patients who claim that they have been harmed by Vioxx are suing Merck (Feder 2004). One of them, Carol Ernst, was awarded \$253.5 million by a Texas jury, which found Merck liable in the death of her husband (Berenson 2005b).⁷ This figure included \$24.5 million for non-economic losses, and \$229 million punitive damages. Not coincidentally, \$229 million is a 2001 Merck estimate of how much additional profit it would make if it could delay an FDA warning label regarding cardiovascular risks (Berenson

2005c). Furthermore, the FDA is being attacked for its supposedly lackadaisical regulation of Merck. US Senator Charles Grassley, R-Iowa, has strongly criticized Merck, FDA, and the “cozy” relationship between them (US Senate Committee on Finance 2004). The Government Accountability Office (GAO), in response to the concerns of Grassley and others, conducted an investigation into the FDA’s ability to perform adequate postmarket safety evaluations; it concluded that “FDA lacks clear and effective processes for making decisions about, and providing management oversight of, postmarket safety issues” (GAO 2006). The end of the scandal will not be seen for years.

III. The Epistemic Inadequacies of the Research on Vioxx

What exactly went wrong in the Vioxx affair? Was the research on Vioxx conducted in an epistemically responsible fashion? This is, of course, a possibility; just because a scientific community or corporation adopts a hypothesis that turns out to be wrong does not imply that the research was epistemically faulty. Were there changes that could have been made that would likely have prevented some of the mistakes from occurring? If so, what were these changes? If the research on Vioxx was not conducted in an epistemically responsible fashion, was this due primarily to the actions of individuals or to institutional failures? The answers to these questions, I will argue, are clear: the research on Vioxx was epistemically inadequate, and the primary cause of this was faulty institutional arrangements.

While many reasons could be adduced for the epistemic inadequacy of this research, I will focus on two. The first is that, between 2000 (or even earlier) and 2004, Merck consistently mischaracterized the current state of knowledge regarding the possible cardiovascular side effects of Vioxx. The hypothesis that Vioxx did not possess dangerous cardiovascular side effects was, until 2004, uncertain, and Merck *knew* that it was uncertain. Despite this, the company consistently and publicly asserted that Vioxx was safe. Secondly, there are serious questions about whether Merck honestly reported data that was unfavorable to its financial interests. Since the withdrawal of the drug, information has come to light suggesting that Merck scientists did not report all of the cardiovascular events that they should have, thus calling into question at least two of the studies that reflected favorably upon Vioxx.

Merck’s Mischaracterization of the Current State of Knowledge Regarding the Possible Cardiovascular Side Effects of Vioxx

Until Vioxx was taken off the market, Merck maintained that Vioxx does not contribute to cardiovascular problems. Yet, from a very early date, Merck scientists and management officials were well aware that Vioxx was at least potentially dangerous. According to documents obtained during the 2005 Texas civil trial, Merck scientists were aware of the potential cardiovascular risks as early as 1997. “The possibility of increased C.V. events [cardiovascular events] is of great concern,” wrote Alise Reicin, a senior Merck scientist and one of the authors of the VIGOR study, in a 1997 email; “I just can’t wait to be the one to present those results to senior management” (quoted in Berenson 2005c,

online article). Additionally, Edward Scolnick, who was at the time the chief scientist at Merck, admitted in a 2000 email that cardiovascular events “are clearly there”; upon comparing Vioxx and its side effects with other drugs he wrote, “there is always a hazard” (Matthews and Martinez 2004, online article). Furthermore, as discussed in the previous section, Merck officials called a meeting in May 2000 to determine whether to pursue studies that directly investigated the cardiovascular safety of Vioxx. The outcome of the meeting, again, was that Merck decided not to pursue such studies—a decision that corresponded to the wishes of Merck marketing officials. The fact that they called such a meeting in the first place, however, suggests that they were aware that the drug was at least potentially dangerous.

Thus, from around 1997, the hypothesis that Vioxx does not contribute to cardiovascular problems was uncertain, and Merck *knew* it to be uncertain. The only prospective trial on Vioxx prior to APPROVe—VIGOR—presented a correlation without an adequate explanation, and of the retrospective studies that purported to help to explain this correlation, some supported Merck’s hypothesis, while others supported its contrary (Konstam et al. 2001; Mukherjee et al. 2001; Ray et al. 2002). Given that Merck was aware of the potential dangers of Vioxx, the epistemically responsible course of action would have been to ensure that its side effects were investigated. Unfortunately, this is not the course of action that was taken. Instead of performing the clinical trials that could have shed light on the question, Merck chose to remain ignorant, all the while asserting publicly the safety of its drug.⁸ In other words, Merck consistently mischaracterized the current state of knowledge regarding Vioxx’s side effects.⁹

Inadequacies with Merck’s Characterization and Reporting of Data

A second reason why the research on Vioxx was epistemically irresponsible concerns the growing questions over whether Merck honestly reported data that was unfavorable to its financial interests. One of these pertains to the reporting of cardiovascular events in the VIGOR trial. After Vioxx was taken off the market, the *New England Journal of Medicine*, which published the results from the VIGOR trial, began to review the data submitted by the study’s authors. The journal received both a paper copy of the study and an electronic version; both of these reported that 17 heart attacks occurred in the Vioxx group, compared to four in the naproxen group. However, through an examination of both the electronic version of the study and the documents that were made available during the Vioxx litigation, it was discovered that data relevant to cardiovascular risks had been deleted from the final draft of the VIGOR study. Among these data were three additional heart attacks that occurred in the Vioxx group. While it was initially believed that the scientists conducting the VIGOR trial did not know about these three additional heart attacks at the time the paper was submitted, this turned out not to be so. A July 5, 2000 memorandum that was obtained by a subpoena during Vioxx litigation showed that at least two of the study’s authors were aware of these heart attacks at least two weeks before submission (Curfman, Morrissey, and Drazen 2005). As a result of the omission of this data, the *New England Journal of Medicine* published an expression of concern regarding the VIGOR study (Curfman, Morrissey, and Drazen 2005).¹⁰

In addition to the questions over the reporting of data to the *New England Journal of Medicine* for the VIGOR trial, there are also serious questions regarding the data submitted to the *Annals of Medicine* for a trial known as “Advantage.” The Advantage trial was a 12-week long, randomized, controlled trial; the resulting study was entitled, “Gastrointestinal Tolerability and Effectiveness of Rofecoxib versus Naproxen in the Treatment of Osteoarthritis” (Lisse et al. 2003). The study was of little scientific value, as the VIGOR trial, which was significantly longer and larger than the Advantage trial, compared the same two drugs. It was, even on the admission of Edward Scolnick, the senior Merck scientist, a “marketing study” (Berenson 2005a).¹¹ It was completed in 2000 but was not published until 2003; several other journals refused to publish the article because of its lack of novelty (Berenson 2005a). The paper was written by Merck; the lead author of the paper, Dr. Jeffrey R. Lisse of the University of Arizona, was paid to put his name on the paper.¹²

Questions concerning the data contained in the article surround the number of patients in the Vioxx group who suffered heart attacks or sudden cardiac death. The article that appeared in *Annals* reported that five patients in the Vioxx group suffered heart attack or sudden cardiac death, as compared to one in the naproxen group. This difference is not statistically significant. It appears, however, that at least one, and possibly three, more deaths in the Vioxx group resulted from cardiovascular problems. For example, a 73-year-old woman in the Vioxx group died while participating in the trial, and when she was examined for cause of death, the Merck scientist who examined her, Dr. Eliav Barr, determined that she died of a heart attack (Berenson 2005a). According to company emails, however, Dr. Alise Reicin, Merck’s vice president of clinical research, repeatedly encouraged Barr to change his original classification; “I would prefer unknown cause of death so that we don’t raise concerns” (quoted in Berenson 2005a, online article). The cause of death was eventually changed to “unknown.” Had it been classified as a heart attack, the difference in CV events between the Vioxx and naproxen groups would have been statistically significant.

Dr. Lisse, the lead author of the Advantage paper, maintains that he never heard of this dispute over cause of death. “Merck designed the trial, paid for the trial, ran the trial,” he said. “The initial paper was written at Merck, and then it was sent to me for editing. ... Basically, I went with the cardiovascular data that was presented to me” (quoted in Berenson 2005a, online article). Thus, while more information regarding the data presented in the VIGOR and Advantage studies needs to be collected, there are strong reasons for believing that the data submitted by Merck was not completely reliable.

Thus far, I have presented two reasons for believing that Merck’s research on Vioxx was epistemically irresponsible. Merck consistently mischaracterized the current state of knowledge regarding the possible cardiovascular side effects of Vioxx, and there are growing concerns over whether Merck honestly reported data that was unfavorable to its financial interests. To these reasons, one could add a third that centers on FDA’s failure to fulfill its regulatory duties. Throughout this affair, the FDA did very little in the way of regulating Vioxx. Not only this; in a decision that I will discuss later, an FDA advisory committee, in February 2005, recommended that Vioxx be put back on the market (Center for Science in the Public Interest 2005). While there is much that is still

not known about FDA's involvement in the Vioxx affair, there are many reasons, some to be discussed later, that suggest that FDA failed to subject Merck's claims about Vioxx to adequate critical scrutiny.

IV. But Aren't these Moral, Rather than Epistemic, Failings?

One could object to my argument thus far on the grounds that Merck's activities represent not *epistemic* but, rather, *moral* failings. Merck officials knew that Vioxx was at least potentially dangerous, yet they refused to conduct the safety trials that could have shed light on the situation, and the public face of the company continued to assert unambiguously the cardiovascular safety of the drug. Doesn't this suggest a moral, rather than an epistemic, failing? Isn't this the domain of ethics rather than social epistemology or the philosophy of science?

My answer to this challenge is to deny a strict distinction between the moral and the epistemic.¹³ It is certainly true that there were moral dimensions to Merck's epistemic failures. As noted, FDA officials estimate that as many as 55 000 patients might have died as a result of taking Vioxx (Harris 2005); even if this figure is inflated, it is clear that many deaths could have been prevented had appropriate safety tests been conducted at an earlier date. But Merck's mischaracterization of the state of knowledge regarding the safety of Vioxx and its apparent failure to report troublesome data also constitute epistemic failings. In the VIGOR trial, a correlation between Vioxx and cardiovascular events was observed. One possible explanation for this correlation—that naproxen has cardioprotective effects and that Vioxx has no cardiovascular side effects—was adopted without adequate empirical justification. The failure to investigate sufficiently this potential explanation, especially given that other studies were casting doubt upon the safety of Vioxx, is clearly an epistemic failing; the fact that it has a moral dimension does not detract from its epistemic character.

The research on Vioxx, therefore, was epistemically problematic. What is the appropriate response to this? Should we chastise the individual scientists participating in this research for their lack of balance and for failing to take up the criticisms of others? Should we require them to take courses in research ethics? Well, perhaps. But these responses are far from sufficient. The *primary* cause of the problematic character of the research on Vioxx—the primary cause of the epistemic/moral inadequacies of the research—was a social one, namely inadequate institutional arrangements. The institutional environment of the research on Vioxx emphasized the short-term financial interests of Merck above almost all else—above the demand for rigorous science, and above the health and well-being of patients. What were these inadequate institutional arrangements, and how did they lead to epistemic failings?

V. Epistemic Inadequacies as Problems of Organization

The first, and perhaps most obvious, inadequacy concerns the organization of Merck itself. As noted, executives at Merck met in May 2000 to discuss the question of whether to conduct further trials on the cardiovascular safety of Vioxx. Yet after input from

both company scientists *and marketing officials*, who argued that there was “no compelling marketing need for such a study,” Merck decided against performing further trials (Berenson et al. 2004). If for-profit corporations are to be relied upon to conduct reliable scientific investigations, they should not allow marketers to have input into scientific decisions. There is no legitimate reason for allowing marketers to be involved in such decisions; in explaining why many contemporary pharmaceutical companies do allow them to have such input, it is hard to come to any conclusion except that such companies value profits over rigorous science. I should emphasize that I am not suggesting that private, for-profit corporations cannot conduct reliable scientific inquiries. Bell Labs was a paradigm example of a company that, on the whole, made striking scientific innovations. But Bell Labs allowed their scientists a relatively high degree of autonomy; this is not the case with most contemporary pharmaceutical companies.¹⁴

Another organizational inadequacy is the lack of independence of the FDA from the pharmaceutical industry. This lack of independence comes in a variety of forms. One of them is the increasing number of FDA officials or advisory committee members who have financial ties to pharmaceutical companies. For example, in September 2000, *USA Today* published a study of 18 FDA advisory committees, consisting of approximately 300 individuals (Cauchon 2000). These committees performed a variety of advisory functions, including recommending how a study should be designed, whether a drug should be approved for sale, whether a drug should receive a stronger warning label, and whether a drug should be taken off the market. Of the 159 committee meetings analyzed between January 1998 and September 2000, 55% consisted of groups in which at least half of the FDA advisors had financial conflicts of interests. These conflicts included the evaluation of a drug that they had helped a pharmaceutical company to develop and consulting for or owning stock in the company that owned the drug they were evaluating. Furthermore, at the 102 meetings that dealt with the fate of a specific drug, 33% of the committee members had a financial conflict of interest.

How might these financial conflicts of interest have affected FDA’s regulation of Vioxx? The presence of these conflicts of interest tends to predispose FDA officials or advisory committee members toward pharmaceutical companies and their products.¹⁵ In such a climate, the presence of such conflicts increases the probability that a committee would make decisions that were in the interests of pharmaceutical companies. One example of this is the recent recommendation by an FDA advisory committee to put Vioxx back on the market (Center for Science in the Public Interest 2005). The committee that made this recommendation consisted of 32 voting members. The vote in favor of putting Vioxx back on the market was 17 to 15. Ten of these committee members had financial conflicts of interest with at least one of the pharmaceutical companies that had drugs under examination—namely Merck, Pfizer, and Novartis. Of these 10, nine voted in favor of putting Vioxx back on the market. Had these 10 individuals abstained from voting, the committee vote would have favored keeping Vioxx off the market.

There are other ways in which the FDA is not sufficiently independent of the pharmaceutical industry. Since 1992, pharmaceutical companies have been required to pay “user fees” to the FDA in order to help to cover the costs of drug approval (Hilts 2003).

This financial dependence of the FDA on the pharmaceutical industry has increased the influence of the industry over FDA regulatory practices. Since 1992, the percentage of FDA money provided by the federal government has been declining, while that provided by industry has risen steadily (Harris 2004). The increasing dependence upon industry money has led FDA to shift its priorities increasingly away from the postmarket safety testing of drugs and toward the approval of new drugs. For example, while the total amount of funding to FDA has remained approximately the same, the percentage of funding devoted to the approval of new drugs has risen from 53% in 1992 to 79% in 2003 (Harris 2004).

The increasing inability of the FDA to handle the surveillance of drugs that are already on the market has made the agency increasingly reliant upon drug companies to report adverse events. In some cases, pharmaceutical companies—as a condition of the approval of their drug—agree to conduct certain postmarketing tests of their drug. Yet, a significant percentage of these are never completed, and many are never even initiated (Fontanarosa, Rennie, and DeAngelis 2004; GAO 2006). Furthermore, when they do conduct their own studies, companies often disregard worrisome effects or fail to conduct the studies that would most clearly show the effects of their drugs (e.g. Angell 2004; Avorn 2004; Krinsky 2003). Certainly, the questions concerning Merck's handling of the cardiovascular data on Vioxx inspires no confidence that drug companies can reliably and effectively evaluate the safety of their own drugs.

Thus far, I have argued that the research on Vioxx was epistemically problematic and that the primary cause of this was inadequate institutional arrangements. What kind of social theory of science can explain this affair?

VI. Lessons for Social Epistemology

Earlier in the essay, I discussed two reasons for believing that the proposals of Kitcher and Longino are inadequate for helping us solve the problems presented by the privatization of science. In this section, I will discuss some of the lessons for social epistemology suggested by the Vioxx case study. This will yield further reasons for questioning the adequacy of the proposals of Kitcher and Longino, and it will provide a helpful basis for making an alternative recommendation for organizing certain aspects of pharmaceutical research.

Examinations of the actual institutional arrangements of science, such as the Vioxx case study, can help to illustrate a number of shortcomings in the ideals of both Kitcher and Longino; I will mention just two.¹⁶ The first is that such examinations raise serious worries regarding the practical attainability of these ideals. To see this, let us consider very briefly Longino's characterization of an ideal scientific community. Two of the four conditions that an ideal community has, according to Longino, are the uptake of criticism and a tempered equality of intellectual authority (Longino 1990, 2002a). The former condition requires that individual scientists take up one another's criticisms—that is, that they listen and respond to the criticisms of others in an open-minded fashion. The latter condition requires that communities not only welcome, but also cultivate, all relevant perspectives on any given issue, and that the individuals embodying these

perspectives interact with one another on an equal playing field. Clearly, these conditions were not met in the Vioxx case. But examinations of the actual institutional arrangements of science, such as the Vioxx case study, raise the following crucial questions. Which organizational arrangements are conducive to individuals interacting with one another on an equal playing field? How is a community to identify “all relevant perspectives” on a given issue? By which procedures can a community cultivate all relevant perspectives? How, especially given the ongoing privatization of science, can we ensure that economic interests do not lead to the privileging of one set of perspectives over another? Are there *any* organizational arrangements that are conducive to the fulfillment of these requirements? These are important questions, for if Longino cannot specify organizational arrangements that result in the fulfillment of her four conditions—if she cannot tell us, in a very specific way, how we are to achieve communities that meet these conditions—then we have little reason to believe that her ideal is achievable, even in principle.¹⁷

In addition to questioning the practical attainability of the ideals of Kitcher and Longino, examinations of the actual institutional arrangements of science also raise serious worries regarding the adequacy of the ideals themselves. For example, one significant problem with both ideals—a problem that becomes clear when analyzing cases such as the Vioxx research—is that they fail to acknowledge the significance of vast power differentials in science.¹⁸ The ideals of both Kitcher and Longino require that scientists—and, in Kitcher’s ideal, lay deliberators—interact with one another on an equal playing field. Both ideals appeal to an imaginary space of reasons in which decisions are made purely on the basis of rational argumentation and in which power differentials—including differences of political and economic standing—play no role. But not only do Kitcher and Longino provide no reasons for thinking that such communities are realistically attainable; examinations of actual institutional arrangements suggest that an adequate social epistemology should acknowledge, in explicit fashion, the role that power differentials play in science. The reason why we are witnessing such a proliferation of scandals in the areas of corporate-funded pharmaceutical research is because private companies have become increasingly adept at using their financial resources to structure the entire research process in their favor. In more and more cases, for-profit entities are funding research, determining the methodologies of research, collecting and interpreting data, writing the reports of the research, and funding—and in some cases, entirely paying for and editing—the journals that publish the research (Angell 2004; Krinsky 2003). Regulatory agencies have increasingly little power over private companies, as such agencies are dependent upon corporate funding and upon advisory committees that are stocked with scientists tied to those companies.

To take just one example of the power that a company can have over large segments of the research process, consider again Merck’s Advantage study, which compared the effects of Vioxx and naproxen (Lisse et al. 2003). This study was created by Merck’s marketing department as a tool to introduce doctors to Vioxx (Berenson 2005a). It was funded by Merck, designed by Merck, and conducted by Merck. Merck scientists collected the data for the study, and when one of its own scientists, Dr. Eliav Barr, determined that the cause of a woman’s death was a heart attack, another more senior Merck

scientist, Dr. Alise Reicin, stepped in and urged Barr to reconsider. The cause of death, again, was eventually changed to “unknown.” Merck wrote the resulting study and then sent it to a prominent university scientist, Dr. Jeffrey R. Lisse of the University of Arizona, who was paid to edit and to put his name on the paper. He maintains that he never saw the original data and that he was unaware of any controversies surrounding the causes of patients’ deaths. And there is no reason to doubt him; the practice of a company collecting its own data, interpreting that data, and sending it to a university scientist to gain an air of authority is now a common practice (Angell 2004; Krinsky 2003).

So what should be done about such situations? Should we simply continue to insist that all parties to this research interact with one another on an equal playing field? Should we merely chastise Merck for using its economic power to skew the research process in its favor? Surely these responses are insufficient. Rather than postulating ideals of imaginary spaces in which differentials of power play no role in scientific research, we should work toward designing systems that institutionalize certain types of criticism and that, more generally, counteract the power of entities that have large financial stakes in the outcomes of research. As is apparent by cases such as the Vioxx episode, not all institutional arrangements are conducive to the kinds of critical exchange, or organized skepticism, that epistemically rigorous research requires.¹⁹ The crucial question, then, is: which kinds of organizational arrangements are conducive to such critical exchange?

In the remainder of this essay, I will discuss briefly one potential answer to this question, namely instituting an adversarial system of research within the FDA.²⁰ Under this system, two groups of advocates would argue before a panel of judges over such questions as whether—and under what conditions—a drug should be allowed on the market, and whether a drug that is already on the market should remain so. One set of advocates would consist of industry or industry-sponsored scientists who would argue on behalf of a pharmaceutical company. The other set would consist of scientists who receive no funding from pharmaceutical companies; these advocates would argue on behalf of the public that, for example, a given drug is sufficiently dangerous that it should be taken off the market. The panel of judges could consist, for example, of FDA or university scientists who are independent of any industry that might have a stake in the outcome of the proceedings.

An adversarial approach represents an acknowledgement that more and more pharmaceutical researchers are better viewed as advocates than as disinterested evaluators of research. As greater numbers of scientists develop financial ties to companies, and as companies exert greater and greater control over the research process, pharmaceutical research becomes an ever more interested affair. Rather than simply insisting that individual researchers and companies be disinterested, an adversarial approach ensures that industry advocates are confronted with advocates that are informed by a different set of interests, namely the interests of public health and welfare. Thus, through its enforced adversarial proceedings, an adversarial approach ensures that industry and industry-sponsored research receives a high degree of critical scrutiny.

This proposal differs from the ones provided by Kitcher and Longino in a number of ways. I will mention only three. Firstly, the proposal is not a general one that is meant

to apply to all areas of science. It is a local one that arises out of a specific set of issues facing a specific community. Again, the epistemic issues in the arena of pharmaceutical research are quite different than those in other areas of science, especially areas that are not so tied to Wall Street. As a result, there is little reason to believe that the organizational arrangements that can best ensure reliable pharmaceutical research would be necessary in other areas of research. The proposal of an adversarial system acknowledges this, as it is meant to apply only to pharmaceutical research.

A second difference between the proposal for an adversarial system and those of Kitcher and Longino is the relatively experimental character of the former. The proposal of an adversarial system is not developed primarily on the basis of reflections about the nature of knowledge, but on the basis, again, of a specific set of issues facing a particular area of science. As a result, the test of the proposal should not be, for example, whether it coheres with our intuitions about knowledge but, rather, whether it can be articulated in a clear fashion, whether it can be implemented, and whether it improves the quality of pharmaceutical research. A more complete argument on behalf of an adversarial system, thus, would require highly concrete discussions of how the system is to be implemented, as well as examinations of previous attempts to implement adversarial systems of research.

Thirdly, the proposal for an adversarial system is, in some sense, more social than the proposals of either Kitcher or Longino. Kitcher's ideal of well-ordered science depends upon the ability of individual scientists to evaluate research, even research that is transiently underdetermined, in a thoroughly disinterested fashion (Kitcher 2001). Longino's ideal, while it does not require individual scientists to be disinterested, nonetheless requires that they listen and respond to the criticisms of others in a thoroughly open-minded fashion (Longino 1990, 2002a). The proposal for an adversarial system, however, requires neither disinterestedness nor open-mindedness to all other perspectives *at the level of the individual*. Rather, it acknowledges that each set of advocates will be just that—*advocates*; through its enforced critical interaction and organized skepticism, it allows objective decisions to arise out of a set of social processes.

VII. Conclusion

In this paper, I have attempted to accomplish two aims. The first was to show that the privatization of science should be an important item on the agenda of social epistemologists. I have argued that the research on Vioxx was epistemically problematic and that the primary cause of these inadequacies was faulty institutional arrangements. This case study, thus, provides further reasons for believing that the privatization of science, at least in the biomedical sciences, is presenting serious epistemic costs, and it suggests that the primary response to this situation should be an organizational one.

Secondly, I have discussed which kinds of social, or organizational, responses would be most beneficial. I have argued that the social epistemological proposals of Kitcher and Longino are inadequate for dealing with the phenomenon of privatization, in part because their proposals fail to take into account crucial features of the ways in which scientific research is actually structured. A more detailed look at the actual organization

of research suggests that social epistemologists should allow an explicit role for power relations in proposals for organizing research.

Partly on the basis of the Vioxx case study, I have discussed a preliminary proposal for reorganizing certain aspects of pharmaceutical research, namely by instituting an adversarial system of research within the FDA. While this proposal requires much more discussion than space allows in this essay, it is a pursuit-worthy proposal that deserves attention by social epistemologists.

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Notes

- [1] This is the theory behind the Bayh-Dole Act of 1980. For discussion of this piece of legislation, as well as others that facilitated the present trends towards privatization, see Krinsky (2003) and Slaughter and Rhoades (1996).
- [2] See, for example, Angell (2004), Avorn (2004), Bekelman, Li, and Gross (2003), Brown (2000, forthcoming), Cho and Bero (1996), Friedberg et al. (1999), Krinsky (2003), and Stelfox et al. (1998).
- [3] Exceptions to this unfortunate trend include Brown (2000, forthcoming), Carrier (forthcoming), and Wilholt (forthcoming).
- [4] Kitcher has also addressed the issue of organization in his book (1993).
- [5] See, for example, Biddle (2006), Brown (2004), Kourany (forthcoming), Solomon (2001), and Solomon and Richardson (2005). For an exchange between Kitcher and Longino, see Kitcher (2002a, 2002b) and Longino (2002b, 2002c).
- [6] This press release can be accessed on a number of websites. See, for example, <http://www.pslgroup.com/dg/1FC1E2.htm> (accessed June 1, 2006).
- [7] Although the jury awarded the widow \$253.5 million, Texas law has caps on the amount of punitive damages that can be awarded to a plaintiff; as a result, Ernst received only \$26.1 million.
- [8] This phenomenon of companies choosing to remain ignorant about certain questions that, if answered in a certain way, would be detrimental to their economic interests is also pointed out by Brown (forthcoming).
- [9] Merck’s lack of candor with regard to the safety of Vioxx is the subject of a revealing warning letter from FDA to Raymond V. Gilmartin, the then-President and CEO of Merck, on September 17, 2001. See Abrams (2001).
- [10] In March 2006, a response by the non-Merck VIGOR authors to the expression of concern was published in the *New England Journal of Medicine* (Bombardier et al. 2006). No

corrections were provided. In response to this, the journal reaffirmed its expression of concern. For further details, see Curfman, Morrissey, and Drazen (2006).

- [11] Marketing studies, which provide no novel scientific information and, in some cases, do not meet standard norms of scientific procedure, constitute a growing segment of many pharmaceutical companies' research agendas. In many cases, a company's primary purpose in performing such studies is to expose doctors to its drugs, to get them into the habit of prescribing its drugs, and to create brand loyalty among patients. The Advantage trial, for example, was created by Merck's marketing department "as a promotional tool, to introduce about 600 doctors to Vioxx" (Berenson 2005a). For additional details on the increasing prevalence of marketing studies, see Angell (2004).
- [12] Ghost-writing is another tactic that is becoming increasingly common in pharmaceutical research. For further details, see Krinsky (2003) and Angell (2004).
- [13] There is now a literature in philosophy on moral epistemology. See the essays collected in DePaul and Zagzebski (2003).
- [14] See, for example, Chapter 9 of Angell (2004), in which she discusses the systematic influence of marketers on pharmaceutical research.
- [15] See the literature cited in footnote 2.
- [16] I criticize the ideals of Kitcher and Longino in much more detail in Biddle (2006).
- [17] Kitcher's ideal faces similar difficulties. For example, Kitcher's ideal begins with a set of ideal deliberators who are somehow representative of the public. Again, these deliberators discuss, among other things, their preferences for which lines of research should be undertaken and then, in consultation with ideal, disinterested experts, settle upon a list of specific research projects. But this ideal, among other problems, simply glosses over the problem of how we are to involve the public in scientific decision-making. The ideal begins with a set of ideal deliberators who are somehow representative of the public, and thus simply assumes, from the start, that the public is involved in an appropriate way. The real-world problem of how the public should participate thus does not even arise. For further discussion of Kitcher's ideal, see Biddle (2006), Brown (2004), and Longino (2002b, 2002c).
- [18] Both Don Howard, in a 2002 reading group on Kitcher's *Science, Truth, and Democracy* at the University of Notre Dame, and Miriam Solomon (2001, 144) have made this point as well.
- [19] Organized skepticism, of course, is one of Robert K. Merton's (1942) famous norms of science.
- [20] James B. Conant was a prominent proponent of a version of an adversarial system of science in the 1950s (see Conant 1951, 1952). Arthur Kantrowitz proposed a different version in the 1960s and 1970s (see Kantrowitz 1967, 1976). I discuss both proposals, and I articulate how such proposals should be modified in the case of pharmaceutical research, in Biddle (2006).

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