In Focus

Lessons in Conflict of Interest: The Construction of the Martyrdom of David Healy and The Dilemma of Bioethics

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Bioethics journals have lagged behind medical and science journals in exploring the threat of conflict of interest (COI) to the integrity of publications. Some recent discussions of COI that have occurred in the bioethics literature are reviewed. Discussions of what has been termed the "Healy affair" unintentionally demonstrate that the direct and indirect influence of undisclosed COI may come from those who call for protection from the undue influence of industry. Paradoxically, the nature and tone of current discussions may serve to dull sensitivities to what is indeed a serious set of issues facing bioethics. Some proposals are presented to address COI and other challenges to the integrity of bioethics and its journals. COI is too important a topic to be left to ideologues, and there is no substitute for readers' caution and skepticism as tools in dealing with the full range of biases that exist in published papers.

Medical and science journals had articles about corporate ties and other potential conflicts of interest (COI) affecting the integrity of publications for decades (Blumenthal et al. 1986; Shapley 1973; Shapley & Kolata 1979) before these issues suddenly came to the forefront of bioethics (Agich 2000; Boyce and Kaplan 2001; Brody et al. 2002; Doerflinger 2001; Elliott 2001; Lopez 2001; Neuhaus 2001; Saletan 2001; W. J. Smith 2000, 2002; Younger and Arnold 2002). Despite formal definitions of conflict of interest (Davidoff et al. 2001) and what has become a voluminous literature on the topic, there is yet no consensus as to what constitutes a COI, an adequate disclosure in particular instances, or a uniformly workable general policy. Operative standards tend to be revised in response to particular challenges, only to be unsettled by the next challenge. This would seem to be a ripe opportunity for bioethicists to restore clarity of vision and moral order to the scientific community, but there is a concern that "In general . . . bioethics is behind the curve on these issues" (Sharpe 2002, 1).

This can be aptly illustrated by following a thread in the bioethics literature that includes two instances of undisclosed conflicts of interest in leading bioethical journals. One undisclosed COI in *Hastings Center Report* has gone unacknowledged, even though the COI was serious enough to warrant a change in editorial policies—that also was left unacknowledged at the time. Moreover, the paper in question has gained considerable attention based on a consistent misrepresentation of its circumstances and implications. Furthermore, commentaries by bioethicists about COI have spilled from scholarly journals to magazines and websites with a heated rhetoric that suggests that discussion has been tainted with a noteworthy ideological agenda. The casual observer is left skeptical about whether bioethicists have their own house in order. Rather than bioethicists being uncritically accepted as teachers and moral exemplars, they may better be seen as unwittingly providing some important lessons, replete with ironies and outright paradox.

David Healy, an Irish psychiatrist at the University of North Wales, figures heavily in the sudden emergence of corporate involvement and COI in the bioethics literature. Particularly in stories about what Carl Elliott (2001, 2004) has dubbed the "Healy affair," Healy has been presented as an exemplary hero and martyr. Arthur Schaefer (2004) has recently declared "No discussion of academic freedom, research integrity, and patient safety could begin with a more disquieting pair of case studies than those of Nancy Olivieri and David Healy" (p 24), Perhaps after reading this present article, readers will agree, but I suspect that if that is the case, the reasons for this assessment will be quite different than outlined in Schaefer's paper.

COI IN *HASTINGS CENTER REPORT* AND *THE AMERICAN JOURNAL OF BIOETHICS*

Carl Elliott helped organize a special issue of the *Hastings Center Report,* "Prozac, Alienation, and the Self," to which Elliott (2000) and David Healy (2000a) each contributed articles. The provocative article by Healy was ostensibly focused on whether antidepressants were being used to treat alienation rather than illness and, if so, should physicians see themselves in a moral quandary. Namely, if physicians used drugs to alleviate the pain of alienation, they might be reducing the spirituality or creativity that go with feeling alienated. The article was also critical of the dangers of antidepressants and it singled out Eli Lilly's Prozac for special criticism: "Arguments in favor of Prozac look more like descriptions of the interests of their proponents than dependable accounts of reality" (Healy 2000a, 21). Healy also claimed that "there are good grounds to believe that

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Prozac (fluoxetine) can trigger suicidality" (Healy 2000a, 21).

Elliott (2001) portrayed the article by Healy and its alleged consequences as the first chapter in what he termed the Healy affair. Shortly after the publication of the article, Eli Lilly withdrew its annual gift of $25,000 to The Hastings Center, with a letter that, according to Elliott, had pointed references to Healy's article and the damage it had done to Lilly's business interests. Elliott noted in passing that Healy had served as an expert witness in lawsuits against Eli Lilly and other pharmaceutical companies by families of persons who had committed suicide and families of murder victims, in which it was alleged that the antidepressants had a causal role in the suicide or murder.

The second chapter of the Healy affair, according to Elliott, was that Healy had a job offer rescinded from the Center for Addiction and Mental Health (CAMH) in Toronto, after a talk in which Healy again made claims that Prozac caused suicide. According to Elliott, the e-mail from CAMH to Healy attributed the rescinding of the job offer to his having an approach that was incompatible with the CAMH clinical and research missions. Elliott noted that CAMH had previously received a $1.5 million-dollar gift from Eli Lilly, but that CAMH had insisted that there was no relation between this gift and the rescinding of the job offer. According to Elliott:

> Whether Lilly or any other corporate funder had anything to do with Healy's dismissal is impossible to know. Even so, the trouble CAMH has had in convincing the public that industry sources were not involved points to the difficulty of discerning financial influence. Would CAMH have dismissed Healy if it had no ties to Lilly whatsoever? Does fear of being unable to attract future corporate money count as influence? Does fear of angering powerful industry-tied psychiatrists? (Elliot 2001)

Healy figures in another article by Carl Elliott about COI, but he is not identified. Namely, Elliott (2003) indicated that according to a paper in the *British Journal of Psychiatry*, some articles concerning Pfizer's antidepressant Zoloft failed to mention significant side effects, including an increased risk of suicide that had been revealed in data released in a law suit. Elliot provides no citation, but perusal of the 2003 *British Journal of Psychiatry* indicates that the article could only be Healy (2003a). According to Elliott, authorship of the questionable articles had been coordinated by a communications agency. Elliott uses this point to illustrate his argument that industry exploits scientific journals as a marketing tool. The relevance to bioethics was that the drug industry was similarly trying to buy bioethicists as authoritative mouthpieces to promote their products while skillfully preserving the bioethicists' appearance of objectivity. That gullible bioethicists continued to believe they were impartial after receipt of money from the pharmaceutical industry was crucial to the success of this marketing strategy. Elliott concluded:

> So the next time you meet a bioethicist, pay close attention; he may look like a bioethicist, but when you peel back his mask, you just might see the adman smiling back. (Elliot 2003)

Another of Healy's writings in *The American Journal of Bioethics* becomes significant in this context because Healy was subsequently identified as having a undisclosed COI, serious enough to warrant a change in the journal policies. Healy contributed an open peer commentary in a discussion concerning the ethics of placebo-controlled trials (Healy 2002). It was only at the end of his commentary that Healy responded to the target article, indicating that he agreed with the authors' (Miller and Brody 2002) methodological points. However, the bulk of the commentary is a seemingly tangential report of Healy's reanalysis of clinical trial data obtained from the U.S. Food and Drug Administration for drugs licensed as antidepressants during the 1990s, findings reported elsewhere, but with different conclusions (Khan et al. 2000).

The original Khan et al. (2000) article concluded there was *no* difference in suicide rates between patients given an antidepressant and patients given a placebo. However, without noting these findings, Healy indicated that he had altered the data in Khan et al.'s tables based on information he obtained through the Freedom of Information Act. In reanalysis, one antidepressant is three times more likely than a placebo to be associated with suicide. No statistical analyses were presented, and the details of how analyses were conducted were so vague that is would be impossible for a reader to reconstruct them.[1] Healy concluded that the ethical issue in clinical trials is not the lack of benefit for patients receiving a placebo, but the risk of suicide associated with patients being given an antidepressant, thus bringing this long digression back to the issue of placebos.

A subsequent editorial in *The American Journal of Bioethics* (Carroll and McGee 2002) revealed that Healy's commentary had an undisclosed COI, in violation of established journal policies. Healy had been receiving money from at least one pharmaceutical company that had a financial interest in the issues being discussed. The editorial took these breaches as a wake-up call for a tightening of COI policies.

1. Asked for details as to how he decided to alter the published data, Healy replied, "Having inside info that some of the 'placebo' suicides and suic [sic] Acts occurred during washout (withdrawal from prior drug) I have simply eliminated them" (personal communication, June 15, 2002)

Healy later revealed that his ties to the pharmaceutical company Pharmacia had figured heavily in the CAMH and University of Toronto's efforts to recruit him (Fraught 2002). Healy recently elaborated on this admission:

> For the record, I am not aware of ever concealing my links to Pharmacia or any other pharmaceutical company. The initial overtures to me regarding a post in Toronto came at a meeting sponsored by Pharmacia, set up by individuals within the University of Toronto. Such links may well have looked attractive to the University of Toronto. (Healy 2003b)

He also disclosed extensive ties to other pharmaceutical companies and involvement in legal action against some companies (Healy 2003c). Separately, Healy attempted to have his reanalyses of the FDA data that had been presented in his *The American Journal of Bioethics* commentary entered as evidence in a trial (*Miller v. Pfizer Inc.*). The publication of his results in the peer reviewed *The American Journal of Bioethics* might be interpreted as giving these data added credibility, but the judge excluded the data and dismissed Healy as an expert witness, in large part because his analyses could not be independently replicated (Toxic Law 2002).

I have personally attempted to provide a commentary on these issues in the *Hastings Center Report*. I wrote to the journal, gave some background on the Healy article in the *Report*, and inquired whether a letter that discussed Healy's undisclosed COI would be considered for publication. Editor Gregory Kaebnick replied:

> Bette Crigger, editor of *HCR* at the time we published David Healy's article, has forwarded your question to me, the current editor. *HCR* now explicitly asks authors to address any conflicts of interest. We had no official policy at the time we considered whether to publish Healy's article, but we did nonetheless expect that our authors would come clean about any financial considerations that readers could reasonably suppose might have prejudiced their thinking. And we probably would have included some note about Healy's role as an expert witness against Lilly. Some financial conflicts of interest we would consider simply to disqualify a piece from consideration; that would certainly not have been the case with Healy's piece. (personal communication, October 12, 2001)

I renewed my offer (J. Coyne, personal communication, October 12, 2001), but this was not accepted. Kaebnick replied: "Obviously we agree with you that there was a conflict of interest that merited publication. Our official policy concerning conflict of interest was spurred by this." However, no acknowledgment of Healy's COI or of the change in policy was provided in the pages of the *Report*. Arguably, the responsibilities of the editor of *Hastings Center Report* went beyond discretely changing the journal's COI disclosure policy. The Draft Code of Conduct for Medical Editors (R. Smith 2003) is clear on its recommendation for these kinds of situations:

> Cogent critical responses to published material should be published unless editors have convincing reasons why they cannot be. (Journals are advised to create electronic means of responding so that "lack of space" is no longer a convincing reason for not publishing a response.)

In the interest of upholding transparency, there would also seem to be a need to correct the public record and to alert readers to factors affecting the credibility of the *Report* and the vulnerability more generally of bioethics journals to undisclosed COI. Such an appearance of a cover up of problems with conflict of interest at another scholarly journal would presumably be newsworthy and suitable for revelation in the pages of the *Report.* Indeed, the *Hastings Center Report* has recently revisited the question of Conflict of Interest, editorializing in its most recent issue that the *Report* is independent even from The Hastings Center itself, an odd claim given that subscriptions to the journal are sold as "associate memberships" in the Center.

I drafted a letter to *American Prospect* where Carl Elliott had given his account of the Healy affair, and as a courtesy I provided Elliott with a copy. I pointed to Healy's financial interests and briefly identified flaws in Healy's assertions that Elliott had uncritically praised. My letter concluded:

> I wonder if Dr. Elliott would like to revise his account of the Hastings Center caper? Might he concede that his bad judgment may have been damaging to the credibility of the *Hastings Center Report* and may given Healy the added claim of having "results" published in *Hastings Center Report* in his promotion of the interests of an Evil Pharmaceutical Company and his own consulting activities? (J. Coyne personal communication, October 11, 2001)

The letter was never acknowledged by *American Prospect*. Elliott replied (personal communication, October 11, 2001): "Thanks for letting me see this. I do hope the *Prospect* decides not to publish it, because it misses the point entirely. Neither Healy's talk at the CAMH nor his article in the *HCR* was about Prozac and suicide."

SE NON E VERO, E BEN TROVATO: CONSTRUCTING DAVID HEALY AS HERO AND MARTYR

The ethical world constructed by Carl Elliott, and more recently by Arthur Schaefer (2004), is refreshingly simple: Heroic academics who courageously speak out against the evils of Pharma get mysteriously struck down, but probably as the result of corporate influences on academia. Bioethics journals that benefit from even modest corporate support face the dilemma of whether to give industry critics a forum and face loss of funding or to reject papers from "independent" critics in order to preserve their funding.

Could there be a simpler, more instructive moral cautionary tale with a clearer message about how big corporations inevitably compromise the integrity of bioethics? Yet, the lessons to be drawn from what Elliott has constructed as the Healy affair may be different than Elliott and others have depicted.

In accepting a legal settlement from CAMH, Healy announced that pharmaceutical companies played no role in rescinding the CAMH job offer. Going beyond the terms of the settlement, Healy now has stated he has never claimed that Lilly or other pharmaceutical companies intervened[2] (Fraught 2002). Outsiders may never know what went on between Healy and CAMH. Yet, as more information gradually becomes available, it becomes distinctly plausible that a crucial part of what went wrong in Toronto is that a lucrative deal with a pharmaceutical company went bad—one that involved Healy and his own work.

Healy has taken the extraordinary step of posting on a special website, http://www.pharmapolitics.com, a wealth of materials from his dispute with CAMH, including his talk and a letter from administrators of CAMH explaining their rescinding of the offer to him. This letter cites Healy's "casual statements" about thousands of people killing themselves on and because of antidepressants (SSRIs), and indicated that CAMH staff had felt his remarks were "scientifically irresponsible, incompatible with published scientific evidence and hence incompatible with the mantle of responsibility of leadership of a clinical and academic program." It should be noted that Healy was to have directed a clinical program for the treatment of patients with mood disorders. The letter charges a conflict of interest in Healy's statements about the superiority of a specific antidepressant, reboxetine, over SSRIs such as Prozac, Paxil, and Zoloft in a paper in a journal supplement sponsored by Pharmacia, the manufacturer of the supposedly superior drug. Further, the paper was based on a talk Healy gave at a symposium sponsored by that same pharmaceutical company. Replying to Healy's claim that Eli Lilly had intervened in Toronto, Dr. David Goldbloom stated:

> We are grateful for the money Eli Lilly donated to our Foundation as we are grateful to our physicians who donated $500,000 to the Foundation. That does not mean we are beholden any more than you might be with regards to the travel or research support you have accepted from Pharmacia and Upjohn, SmithKline Beecham, Duphar, Astra Zeneca, the Wellcome Trust, and other sources.

Healy had recently touted the superiority of the drug reboxetine over SSRIs in numerous papers (Healy 2000b; Healy & Healy 1998; Tranter et al. 2002) that did not carry acknowledgment of any COI or in particular, the sponsorship of the paper by a pharmaceutical company that served to gain financially from such claims. However, a number of his most recent papers (Healy 2002, 2003c) include disclosures of conflict of interest. One statement is quite extraordinary:

> In recent years Dr. Healy has had consultancies with, been a principal investigator or clinical trialist for, been a chairman or speaker at international symposia for, or been in receipt of support to attend meetings from: Astra, AstraZeneca, Boots/Knoll Pharmaceuticals, Eli Lilly, Janssen-Cilag, Lorex-Synthelabo, Lundbeck, Organon, Pharmacia & Upjohn, Pierre-Fabre, Pfizer, Rhone-Poulenc Rorer, Roche, SmithKline Beecham, Solvay, and Zeneca. Dr. Healy has been an expert witness for the plaintiff in five legal actions involving SSRIs and has been consulted on a number of other attempted suicide, suicide and suicide-homicide cases following antidepressant medication, in the majority of which he has offered the view that the treatment was not involved. Dr. Healy has also been an expert witness for the defense on a series of LSD (46) and ECT (1) cases. (Healy 2003c, 10)

This statement is noteworthy in a number of respects, besides having no precedent in Healy's past papers. Namely, it reveals the limitations of a simple laundry list of past associations with industry as an aid in readers' independent evaluations of possible author biases. No indication is provided as to how substantial or trivial associations might be, or what associations might be recent and relevant, versus what might be long past. The net result is that a reader might conclude that these affiliations are self-canceling, assuring the objectivity of the author. Overall, no good basis is provided for distinguishing between such a situation and a contrasting one in which a single specific tie was substantial, currently operative, and carrying a serious threat to an author's credibility.

2. Healy would seem to be contradicting himself or at least retreating from previous statements. For instance, in a letter to a CAMH administrator he posted on his websites (Healy 2001) he stated, "For my money the likeliest scenario is that considerable pressure was brought to bear on you during the course of Thursday November 30th. Why should some version of that latter option have happened? The story to date has played in terms of Lilly's involvement in supporting CAMH. This has been a reasonable way for the story to run given Lilly's involvement in pulling funding from the *Hastings Center Report* following an article that picked up on the Prozac issues that seem to have so concerned you. I am sure their action is one you deplore, although your letter does not say so. It was a reasonable way for the story to run given that researchers from CAMH were down in Indianapolis on that day talking about research product in return for Lilly funding. However I have never at any point suggested that the CEO of Lilly or anyone else associated with Lilly contacted any one from CAMH on that or any other day."

REBOXETINE VERSUS FLUOXETINE: A MATTER OF POTATOES VERSUS SPUDS?

When Healy was first negotiating a position in Toronto, Pharmacia was making a bold effort to seize a major portion of the multi-billion dollar market for antidepressants. This market was dominated by the SSRIs and Pharmacia was marketing reboxetine, a nonSSRI. Reboxetine had been licensed in 50 countries, but not in Canada or the United States, although it once had a provisional approval in the United States. The U.S. Food and Drug Administration subsequently requested more clinical trial data be collected in the United States for a final approval. In May 2001, the FDA declined Pharmacia's licensing application without offering an explanation. With Canada expected to follow suit, Healy became less useful to the pharmaceutical company and therefore perhaps to CAMH.

Antidepressants are notoriously similar in average efficacy, a point emphasized by Healy in his 1997 book, *The Antidepressant Era*. Market advantage depends on what can be marginal differences in side effect profiles or patient tolerance. Consistent with other research, Healy's own work failed to show that reboxetine was superior to SSRIs (Healy, 2000c). However, with funding from Pharmacia, Healy assumed a strong role in promoting a case for reboxetine's superiority. In a number of symposia and papers supported by the company, he reiterated claims that different classes of antidepressants can be expected to show different mechanisms of action, different effectiveness with different classes of depressed patients, and different side effects. If these claims seemed to be contradicted by a wealth of available data, it was because the standard assessments of outcome in clinical trials were insensitive to these differences. He made this case citing effects obtained with an unvalidated measure of social adjustment—incidentally developed by a drug company. However, carefully reading his papers, one discovers that his results still revealed no significant difference between the drugs, if one relied on conventional statistical analyses. Yet, he went further and claimed that reboxetine has the distinct advantage of not causing suicide, unlike SSRIs,. If it could be accepted that reboxetine had some advantage over SSRIs—or even better, if the large share of the market for antidepressants held by the dominant SSRIs could be reduced by claims that SSRIs cause suicide—there would an enormous windfall for Pharmacia, the manufacturer of reboxetine.

Elliott (2001) relayed Healy's claims from what is undoubtedly the most controversial paper Healy has produced, the so-called the Normal Volunteers study touting the advantages of reboxetine over SSRIs,. Few people have actually seen the original report: it is not indexed in Medline and the journal in which it appears, *Primary Care Psychiatry*, is not carried by many medical libraries. The paper is nonetheless quite interesting in terms of both scientific and ethical standards. The judge who disqualified Healy as an expert witness in *Miller v. Pfizer Inc* specifically cited the flaws in this paper as one of his primary reasons for this action.

In the paper, Healy (2000b) claims to have administered in randomized order reboxetine and an SSRI to 20 volunteers. None were depressed, and all were underlings at a hospital where Healy had administrative responsibilities. Two of the volunteers developed suicidal thoughts while receiving the SSRI, and one of them, a woman whom Healy later identified by name in the press, had difficulty resisting the urge to kill herself by throwing herself in front of an oncoming automobile.

The study was seriously flawed from a scientific point of view. It was allegedly a Phase 1 study of effects of reboxetine on quality of life, but there were too few subjects enrolled to yield the statistical power for a credible test of differences in the drugs. There was no placebo control group, and so the implausible premise of the study became that the drugs would be so strikingly different from each other that the difference would be noticed with only 20 people chosen specifically because they did not have the condition for which the drugs were developed to treat. Given the history of past comparisons of similar drugs, a significant difference under these circumstances would be highly unlikely. The most serious methodological criticism was that research participants were Healy's paid staff who undoubtedly knew his views on these drugs, and their subordinate position with respect to him gave them reason to provide him with the results he desired. The behavior of the two volunteers who developed suicidal ideation was quite bizarre for some time, and apparently was observed by their colleagues and coworkers at Healy's hospital. Healy waited over a week after the behavior became evident before attempting to stop the medication, and even then, he claims that the woman who attempted suicide continued to take the medication because she felt compelled to do so. While it is always important to monitor and ensure the safety of research participants in drug studies, it is considered particularly important when these participants are not expected to obtain any medical benefit. Moreover, it is also curious that when other results from this same study were subsequently reported in another paper (Tranter et al. 2002), there was a detailing of the side effects that the volunteers reported, but no mention of the alleged emergence of suicidalilty or other bizarre behavior that have made this paper so well known.[3] Clearly, if such adverse effects had

3. The only reference to the Healy (2000b) paper in the later paper (Tranter et al. 2002) was a passing notice that some research participants felt calmer on the SSRI while others were agitated.

been observed, there would have been a responsibility to report them in any enumeration of side effects.

What are we to make of this study? Healy has extensive research published in peer review journals, so we can assume he could recognize the scientific and ethical flaws of the study. This may be one of those instances in which reference to COI could have been used to make sense of an otherwise anomalous paper. Namely, Healy had a financial relationship with Pharmacia involving touting the advantages of its product over rivals, and had a role as an expert witness in a civil case for which the results reported in the paper would be crucially valuable. But there was no such disclosure.

IS CONSULTING IN LEGAL ACTION AGAINST THE PHARMACEUTICAL COMPANIES LESS BIASING THAN CONSULTING FOR THESE COMPANIES?

The Revised Uniform Standards for Manuscripts Submitted to Biomedical Journals (Davidoff et al. 2001) specifically refer to retention as an expert witness as a relevant COI, but there has been a marked inattention in the bioethics articles I have discussed to the possibility that Healy's objectivity and even credibility might be affected by the potential payoff for him as an expert witness. Arguably, the threat of bias may be greater for an expert witness than for someone with a nominal tie to industry. There is no ambiguity to the expectation that a paid expert witnesses will espouse a particular view, and the ability of potential expert witnesses to attract compensation is enhanced by their public espousal of particular views useful in ongoing or pending legal actions.

Healy has been retained as an expert witness for a number of cases involving SSRIs by Vickery and Waldner, a Texas law firm that has been involved in at least 14 law suits against Lilly (Swiatek 2000). Vickery and Waldner are one of a number of firms that actively solicit either product liability suits or criminal cases in which use of an antidepressant is claimed as a defense to the charge of murder.

The testimony of an expert witness can be piviotal in these cases. This was well illustrated in the consequences of a judge's exclusion of Healy's expert causation testimony as not meeting *Daubert*'s admissibility standards in a suit alleging that Zoloft, an SSRI, caused the suicide of a teenager (*Miller v. Pfizer Inc.*). After hearing the conclusions of independent experts appointed by the court, Judge Kathryn H. Vratil ruled that there were "glaring and overwhelming" flaws in Healy's methodology. The judge specifically noted inadequacies in Healy's Normal Volunteer Study, including that research participants were aware of his hypotheses beforehand, and that a meta-analysis of the kind Healy presented in *The American Journal of Bioethics*—perhaps the same one—could not be independently replicated (Toxics Law 2002). Because the plaintiff's case depended on Healy's testimony, its exclusion resulted in a summary judgment in favor of Pfizer.

Fees for an expert witness cannot be made contingent on the outcome of a case, but Healy is a repeat player in these legal actions, and future opportunities depend on past performance and a credible, predictable testimony. As seen in *Miller v. Pfizer Inc.*, the credibility depends on the ability to muster evidence that is deemed scientifically valid. One criterion is that the interpretation of data has survived peer review, and the responsibility of a repeat expert witness is to ensure the availability of peer reviewed evidence. Having a basis for a claim of peer review may explain Healy's otherwise odd choice of *The American Journal of Bioethics* for the first presentation of his meta-analysis of data obtained from the Khan et al. (2000) study.

However, Healy's claim of demonstrating that antidepressants induce suicidality in persons who are not even depressed has a more basic role in legal action against pharmaceutical companies: publicity. The law firms specializing in product liability suits involving antidepressants have impressive public relations engines. Vickery and Waldner maintains a website, justiceseekers.com, publicizing the claim that antidepressants cause suicide and homicide and bragging about successful cases. (The defeat in *Miller vs. Pfizer Inc.* is not noted.) The publicity campaign by these law firms targets the media with numerous press releases. These press releases often in turn become news stories that do not disclose their origins. Rampton and Stauber (2001) notes the high proportion of news stories that originate in press releases and estimate that more than half in the prestigious *Wall Street Journal* are based solely on press releases. Rampton and Stauber further note:

> There is indeed a great deal of bad science in the news media and in courtrooms, and not all of it comes from corporations. Over the years, both business marketers and advocacy groups have become highly skilled at inventing and exaggerating fears, dealing in dubious statistics and using emotional appeals to sell products or mobilize public support for causes. The time constraints in visual nature of television make simple messages stand out more easily than complex ones, and marketers have learned to exploit this reality of the modern mass media. (p. 22)

Details are not readily available on the scope of public relations activities of the law firms soliciting product liability suits regarding antidepressants. However, one highly visible firm, Baum, Hedland, Aristie, Guilford, and Downey, operator of www.zoloft-side-effects-lawyer.com, boasts on their website that the publicity effort they were able to mount following September 11, 2001, resulted in over 1,000 requests from the media and representation by the firm of hundreds of the victims.

It is also clear that being a repeat expert witness like Healy in product liability is much more than a matter of serving as a detached scientist pondering the weight of evidence. Sustained success is more assured with the generation of relevant data and participation in a formidable publicity machine. Regardless of whether one accepts Judge Vratil's assessment of the quality of Healy's work, Healy has a vested interest and potentially ample financial reward for getting the credibility of peer review for his work. Carl Elliott indicated in his *American Prospect* article that he was aware of Healy's role as an expert witness in product liability suits. Should this have influenced the decision to include Healy in the special issue of *Hastings Center Report* (2000a) or, at a minimum, should the information relevant to COI have been made available to readers? Is the fact that Healy is actively for hire in litigation any less a reason for concern about his bias than if he had been subjected to pressures from having a tie to a private corporation?

ARE YOU OR HAVE YOU EVER BEEN. . . ?: REFLECTIONS ON ACCUSATIONS OF COI

Bioethicists' discussions of COI spill from *Hastings Center Report* and *The American Journal of Bioethics* to the magazines *American Prospect*, *Slate*, and *Dissent.* Presumably, the standards for evidence, documentation, and argument of bioethics journals are different than those of magazines, but what happens to the standards of the bioethics journals when the magazines are then cited with authority in a bioethics journal (Sharpe 2002)? Furthermore, the reader who follows the thread into the magazines finds a heated rhetoric, raising issues about the ideological bias behind what is appearing in the bioethics journals:

> But do bioethicists really want to brand themselves with Pharma? To take only one example: The pharmaceutical sponsors of the University of Pennsylvania Center for Bioethics and its faculty's projects are now facing multimillion dollar fraud sanctions (AstraZeneca), a Nigerian lawsuit for research abuse (Pfizer), massive class-action payouts (Wyeth-Ayerst), a criminal probe into obstruction of justice (Schering Plough), an ongoing fraud lawsuit (Merck and Medco), and allegations of suppression of research data on suicide in children (GlaxoSmithKline). (Elliott 2003)

An interested reader can try in vain to sort through what exactly is being charged about these companies and to evaluate the charges in light of the available evidence and the relevance, if any to the bioethicists in question. Without relevant evidence, the reader is left assuming a responsibility that belongs more rightly with the author.

From the magazines and newspapers, the claims of these authors further spill to the Internet (e.g., http://www.ahrp.org) where Elliott and Healy post comments interspersed with others' direct quotes from lawyers soliciting clients for legal action against pharmaceutical companies [4] A perusal of the exchanges on the website reveals what a brave new world would be like with only those persons claiming no ties to industry speaking. Journal articles and government reports are routinely dismissed because an author or committee participant has had a known association with industry. On the other hand, claims that antidepressants are addictive are routinely accepted, as if there were a scientific basis for them.

In current discussions of COI in the bioethics journals and by bioethicists elsewhere, there is a radical certainty with respect to the charge of an operative COI and a radical skepticism concerning any denial. Considerable license is allowed in speculating about the how the COI operates, but there is also considerable doubt about the truthfulness of any defense. All of this attention to an author's ties ultimately can become a distraction from what an accused person is actually saying and the need for any critical evaluation.

It is a simple matter to charge conflict of interest, and there are no ready means of refuting such a charge, particularly when one holds to the principles of radical certainty of accusation and radical skepticism toward denial or explanation. Yet, if one accepts the definition of the Revised Uniform Standards for Manuscripts Submitted to Biomedical Journals, it is not hard to uncover a *potential* conflict of interest for anyone. Discussion of an alleged COI can readily become a *tu quoque*. One can, for the sake of argument, charge that Carl Elliott is making a fuss about the "Healy Affair" in order to publicize his forthcoming book, *Prozac as a Way of Life* (Elliott and Chambers 2004), in which Elliott and Healy each have a chapter. How can that charge be refuted? And one can escalate: if Elliott is concerned about institutional COIs, why has Elliott been so silent about the University of Minnesota's Institute for Applied and Basic Research in Surgery (IABRS; See Krimsky's 2003 scathing account of this program)? Is Elliott avoiding the embarrassment of his bioethics center's benefiting directly and indirectly from the millions of dollars IABRS obtained for the University of Minnesota from the illegal sale of drugs?[5] We now have some more easily made but difficult to eliminate charges on the table and we are that much less likely

4. See, for instance, the January 25 2004 posting, ACNP Summary Report Criticized as Junk Science on www.ahrp.org (Retrieved December 2, 2004).

5. According to Krimsky (2003), the University of Minnesota raised millions of dollars for research selling a drug Antiolymphocyte Globulin (ALG) that had never been approved for general use. In 1992, the FDA found 29 violations in the ALG program including "failure to report adverse reactions; failure to monitor studies; unauthorized exports of the drug; numerous gaps in the testing record; and improper claims that the drug's safety had been established (Krimsky 2003, 34).

to get back to evaluating whatever point was being made before the charges started flying.[6]

Recognizing this problem, some scientists have called for sticking where possible with what is being said, rather than the associations of who is saying it. As Stephen Welch (1997, 865) has succinctly put forth this strategy, "Judge the word, not the author." It is often easier to explicate the faults of bad science than come to any firm conclusions about the motives and biases of the scientists, and it is usually more useful.

Perhaps the lopsided focus on the transparency of the financial ties of authors in bioethics journals can be understood in part as a response to a lack of transparency in the writing in the papers that appear there. The papers I have reviewed here suggest that the standards of bioethics journals are such that authors often make seemingly empirical claims without invoking data, cite data without providing sufficient documentation for readers to form their own opinions, and pass on one author's proclamation in a magazine as support for one's own undeveloped argument. It is indeed *ad hominem* when we attack the author rather than his or her arguments. Yet if these arguments are not clearly developed but available only in declarations, if sources are not revealed, and if evidence is not made available, we are left having to depend heavily on our assessment of the author's reputation and credibility. What in ideal circumstances would be irrelevantly *ad hominem* becomes crucially to the point.

SUMMARY AND INTEGRATION: IRONY AND PARADOX

One serious shortcoming of discussions of COI and COI policies for the field of bioethics and its journals is that proponents of stringent standards have not had the benefit of compelling examples of demonstrable bias intruding into the literature as a result of COI. This has yet, for example, to be a parallel to the revelation that Nemeroff and Owens (2002) had made claims in *Nature* contradicted by available data but favorable to a drug manufactured by a company from which Nemeroff could purchase 72,000 stock options for fractions of pennies per option (revealed in Carroll and Rubin 2003).

Those who are skeptical of the importance of bioethics might quip that there is little evidence that industry assumes anyone listens to bioethicists. However, the background I have presented in this article suggests, ironically, that proponents of strict standards have themselves have ended the drought by raining down claims with attached conflicts of interest serious enough to force changes in the editorial policies of two major bioethics journals. Some of those expressing the greatest concern about involvement with industry and other financial interests appear to be themselves guilty of directly and indirectly promoted financial interests. Their ostensibly strong anti-industry bias may actually hide allegiance to particular companies or to parties seeking financial gain in consultative activities associated with expert testimony. Beyond those financial interests, there is a clear ideological agenda that distorts definitions of conflict of interest, that encourages hypocrisy in overlooking biases associated with promoting the sale of expertise relevant to legal action, and, ultimately, alienates all of us who are not reflexively and vehemently negative about all business or psychotropic medication.

Elliott (2003) and Antonuccio and colleagues (2003) have each recently introduced the notion of key opinion leaders (KOLs) into their discussion of COIs. KOLs, according to these accounts, "are recruited by industry to smuggle 'buzz'—by talking casually to colleagues, giving lectures at meetings, speaking to the press, or doing virtually anything else that will garner positive publicity for the drug." According to Elliott (2003), the more discrete and unnoticed the tie to the company, the greater the credibility. KOLs are biased, even if unknowingly, by their pay and serve a useful function in smuggling tainted claims into the literature. Yet, how is this different from Elliott's putting claims about wild behavior of the research participants in Healy's "Normal Volunteer" study in *Dissent* (Elliott, 2004), claims that go far beyond what was contained in the research paper (Healy, 2000c) and that would be invaluable in promoting Healy's work as an expert witness? Unless we are prepared to accept that one degree of separation from the financial reward makes such claims acceptable, it would appear we now need a concept of the "mule" paralleling the concept of KOL. Some mules are paid and not acknowledged for their potential for financial gain, but others are merely unpaid, hapless persons who, because of ideological commitments or other ties, are quite

6. A recent fellow at the Center for Bioethics of University of Minnesota (DeVries 2004) has provided another example of this triumph of the outing of conflict of interest over consideration of substantive issues. Namely, a committee on ethics of the American College of Obstetricians and Gynecologists (ACOG) concluded that physicians are ethically justified in performing an elective cesarean delivery if they believe that procedure promotes the mother's health or well-being. Individual decisions concerning cesarean versus vaginal delivery can become complex, particularly when a cesarean delivery is requested by a well-informed woman. However, DeVries (2004) avoids these complexities by focusing on ACOG having gotten what he viewed as an economically advantageous decision from the ethicists. That from DeVries' (2004, B02) point of view is enough to discredit the ethics committee. The ethics committee's decision becomes the basis for DeVries' title theme of "Businesses are buying the ethics they want" and his enthusiastic invoking of Elliott's statement: "No wonder so many of us are looking around for the exit doors. If this is where American bioethics is heading, it is time to get off the train." As the deputy executive vice president of ACOG later pointed out (Zinberg 2004), DeVries (2004) was mistakenly assuming that physicians receive higher reimbursements for a cesarean delivery, which they do not.

willing to import "buzz" into the literature, listserves, and other professional forums. Are mules more credible than or morally superior than KOLs?

Those arguing against paid involvement with industry and for strict reporting standards claim to be trying to protect the reputation of the field. Yet, ironically, they have embarrassed the field with concealment of conflict of interest, rhetorical excesses, and retreats from concern with what is said to an exclusive focus on who is saying it, and, at times, simple silliness.

Even when well intended, long lists of disclosures of potential conflicts of interest do not seem very effective. As Healy (2002) and Shiffman (2002) have demonstrated, it is easy to use long lists to obscure, rather than reveal, operative influences. Furthermore, unless one assumes that all ties to industry or all receipt of money provide prima facie evidence of equally serious bias, then the list strategy risks reducing the egregious example of an author's getting thousands of stock options for pennies to the equivalence of receipt of a modest honorarium—or, if Sharpe's (2002) suggestion is taken seriously—an author's wife's honorarium four years earlier.

Bioethics is faced with recent intrusions of serious undisclosed conflicts of interest and low quality in discussions of the problem. Perhaps this state of affairs can serve as wake up call for more serious reflection on some larger issues, such as:

1. The focus on disclosure of interest as an "outing" of automatic bias, without any analysis of what constitutes bias suggests a pressing need for an analysis of bias and undue influence and how it can be identified and addressed. Nowhere in the articles I have reviewed was there any attention to how it can be determined that someone is biased—beyond demonstration of a tie to industry or financial gain. An important start tackling this topic could invoke the valuable insights of sociology such as Robert Merton's (1973) four norms of science—universalism, communism/communalism, disinterestedness, and organized skepticism. Psychology also has a rich tradition of empirical research explicating intentions, and unintentional, and unrecognized bias (See, MacCoun 1998a).
2. While it would be hard to argue against the need for some policy regarding disclosure of COI, it is easy to see the drawbacks of unselective lists of associations provided without further explanation. In considering solutions, editors of bioethics journals would do well to consider some adaptation of the recommendations of The Revised Uniform Standards for Manuscripts Submitted to Biomedical Journals:

   > Authors should describe the role of the study sponsor(s), if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the report for publication. If the supporting source had no such involvement, the authors should so state. (Davidoff et al. 2001)

3. Understanding of the nature of the COI operative in the articles I have discussed here requires some technical background that many bioethics editorial boards may not possess. If *The American Journal of Bioethics* appears to have been used by Healy to promote his interests as an expert witness, it was in part because the editor could not evaluate his altering of data. Perhaps editing and reviewing manuscripts for bioethics journals are too important and demanding of specific scientific expertise to be left exclusively to bieothicists, and outside expertise should more routinely be sought. One cannot evaluate a discussion of the alleged dangers of psychotropic medication without some relevant background. Journals need to guard against unsubstantiated assertions about technical matters and the lack of references or explication that allows readers to form their own opinions. The articles I reviewed here suggest there is a distinct risk that bioethicists will be characterized as espousing emotion-laden views about matters they know little about.
4. Analysis of the problem of conflict of interest and formulation of adequate policy of disclosure depends on achieving a deeper understanding of how involvement with industry and government have changed the functioning of universities for better and worse (Bok 2003). A Luddite response is insufficient. For instance, if I want to study how mindfulness meditation can free recovered depressed patients from requiring medication to avoid relapse, the National Institute of Mental Health will likely require that I partner with industry to pay for the medication from which the patients will ultimately be withdrawn. Does receipt of that support invalidate me as a subsequent commentator on the treatment of depression? If I use, as I actually am using, money from the National Cancer Institute to redesign a caregiver intervention so that it is more culturally appropriate and sustainable in the African-American community, NCI will probably not renew my grant unless I come up with a plan for partnering with business for dissemination. These are modest examples of a larger issue: involvement with industry may be a requirement to do things that there are arguably good reasons to do. How do we evaluate such involvement?

The exclusive focus on industry as evil and the source of undue influence can distract us from other undue influences such as the need to espouse particular ideologies in order to obtain government funds. Researchers who produce findings relevant to strategies for decreased use rather than abstinence from use of drugs (e.g., MacCoun 1998b) risk not

getting funded from the National Institute of Drug Abuse. This makes it difficult to evaluate published research findings apparently supporting abstinence. More ominously, the Center for Disease Control has become quite explicit about the ideological requirements of receiving funds. For instance, "None of the funds made available for injury prevention and control at the Centers for Disease Control and Prevention may be used, in whole or in part, to advocate or promote gun control."[7] How do we evaluate the work of authors who are funded by CDC? These are limited examples of much more pervasive issues that are not to be solved with simple lists of funding sources.

Issues of conflict of interest in published papers and to disclosure policies for journals are too important to be left exclusively to ideologues. Furthermore, there are some distinct risks that the way in which conflict of interest is being discussed in bioethics could have some unfortunate paradoxical effects. First, it could lead to an utter loss of distinction or an inability to recognize differences between inconsequential, desirable, or unavoidable involvement with industry or the government and sources of pernicious distortions in what is said about particular issues. Second, there is variously a numbing or off-putting quality to some of the discussion in the bioethics literature, particularly as it has spilled into magazines and the Internet. It would be a pity if the result were that serious scholars came to discount conflict of interest as a legitimate and very much needed area of work.

Finally, if the two major bioethics journals have unleashed undisclosed conflicts of interests on their readership, perhaps this should be a reminder to readers to keep their own level of skepticism set appropriately high. The editors of *Hastings Center Report* chose to keep from readers what they viewed as a significant conflict of interest, and the editor of *The American Journal of Bioethics* only belatedly caught a breach in the journal's existing policy involving an altering of archival data. In setting their level of skepticism, readers should not be lulled into thinking that financial conflicts of interest are always the greatest only threat to the integrity of what they read. Organized in a list, these ties are readily countable, but what is countable does not always yield a noteworthy or meaningful sum, and what matters most may not be countable. "Academic, personal, and political rivalries and beliefs are less easily recognized, but each may affect an interpretation" (Horton 1997). Maybe at some point the quality of writing in the bioethics journals will progress to the point that readers have enough information to judge the words, not the author. But it appears that time has apparently still not arrived.

DISCLOSURES

In recent years, the author has been principal investigator on numerous grants totaling several millions of dollars from the National Institutes of Mental Health, National Cancer Institute, National Heart Lung and Blood Institute, and Department of Defense Breast Cancer and Prostate Cancer Programs. More substantial funds have been received in grants on which the author has served as co-principal investigator or co-investigator from the same sources, as well as from the Lance Armstrong Foundation and the Pennsylvania State Tobacco Settlement Fund. The author has recently been a consultant to projects funded by governmental agencies and nonprofit foundations at University of Pittsburgh, American College of Radiology, University of Virginia, M. D. Anderson Cancer Center, Fox Chase Cancer Center, Wayne State University, University of Toronto, University of Montreal, University of Groningen, and University of Munich, and he has regularly served as a consultant to the National Institutes of Health and Department of Defense Breast Cancer and Prostate Cancer Programs. He received $1,000 for participation in the Depression and Bipolar Support Alliance Consensus Conference on the Diagnosis and Treatment of Mood Disorders in the Medically Ill. The author also received $1,000/year for a three-year term selecting recipients for the Welcome Back Award of Chamberlain Communications.

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7. Elliot (2004, 98) reports that of the 20 normal volunteers taking an SSRI: "One began planning to hang herself from a beam in her bedroom. Another had a recurring dream where she slit her throat in bed and bled to death beside her partner. Both subjects became highly anxious, even aggressive, yet strangely detached from their own actions. One de-scribed the drug she was taking as a "chill pill." She said that she had decided to throw herself in front of a car, and it was only by virtue of a chance phone call that she was stopped. . . . One became uncharacteristically aggressive, at one point jumping out of her car in traffic to manhandle a stranger shouting in-sults from the side of the road."
Lots of questions can be raised if we are asked to accept these descriptions at face. If such behavior was occurring, why was the trial not stopped? Why was such behavior not mentioned in the two reports of the trial in the literature, one of which stated only that the researcher participants felt calmer taking the nonSSRI (Tranter et al. 2002)? If two of 20 "normal" persons taking SSRIs had such dramatic problems, why do we not hear about more problems among the millions who are currently taking such medications?

8. see http://www.cdc.gov/od/pgo/funding/ARs.htm For other egregious examples, see the report by the Union of Concerned Scientists (2004).

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