Conflicting Interests in Toronto

anatomy of a controversy at the interface of academia and industry

David Healy

ABSTRACT In December 2000, the University of Toronto breached a contract it held with me, initiating a sequence of events that has led to a public letter to the University from a large number of senior figures in the psychopharmacology community, protesting against the infringement of academic freedom involved, and a first-ever legal action seeking redress for violation of academic freedom. This case has been intertwined from the start with a longer running debate about the possibility that the SSRI group of antidepressants may have the potential to trigger suicidality or other serious effects in a subgroup of takers. And this specific issue connects to concerns about conflict of interest in the domain of therapeutics, as well as in science in general, the ghostwriting of scientific articles, and a series of other hot-spots on the interface between academia and industry.

Cambridge

It was a scary moment. In July 2000, a guest speaker at the annual meeting of the British Association for Psychopharmacology came up to me at a poster stand, where I was presenting details of one of our studies, and said that I had no right to present research like this. Even when challenged with the fact that there was

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other unpublished data, which amply bore out our findings and conclusions, he still insisted that I should not be presenting research like this. He went on to make it clear that he had been approached to get involved in a set of legal actions "against me." This simply may have meant that he was being consulted about being an expert witness on the other side to me in an SSRI medico-legal case, and his advice could conceivably have been seen as paternalistic—but this is not how it felt at the time.

The study I was presenting was designed in the first instance to explore how antidepressants worked. Given that there are now antidepressant agents selective to different neurotransmitter systems, it is a reasonable supposition that these drugs should have different functional effects. The best group of subjects in which to pick up such effects is a group of healthy volunteers with some interest in behavior. Accordingly, with colleagues, I recruited 20 senior medical, nursing, and administrative staff from the psychiatric unit in which the North Wales University Department was also based. The volunteers were randomized to either sertraline (Zoloft), a selective serotonin re-uptake inhibitor (SSRI), or reboxetine, an agent selective to the norepinephrine system (then unavailable in North America). Subjects were randomized to a clinical dose of one or another of the two agents for two weeks, followed by a two-week discontinuation arm and then randomization to the other agent for two weeks. Could the subjects distinguish the two agents? And if so, could they specify what was functionally different about the two agents? We had a series of other questions, such as whether personality type predicted who would prefer which agent, and predictions as to the differential impact of either agent on quality-of-life scores.

The study found different functional effects between the agents. Reboxetine, the drug selective to the noradrenergic system, increased drive and energy, whereas sertraline, the SSRI, appeared to produce a mellowing of affect. Personality measures did predict who would prefer these differential effects: one-third of our subjects preferred the effects of sertraline, while one-third preferred those of reboxetine. Roughly half of our subjects felt better than well on one or other of the two agents. Those who strongly preferred sertraline did rather poorly on reboxetine and vice versa (Tranter et al. in press). In the case of two of our volunteers, the effects of sertraline were disastrous. They became acutely and seriously suicidal (Healy 2000a).

It was these results that I was presenting at the British Association for Psychopharmacology meeting, along with a preliminary statistical analysis of the association between personality type and responses, as well as the differential impact of the two drugs on quality-of-life measures.

By the time of the presentation, I was aware that our findings were not unique. More than 15 years beforehand, Pfizer had run a study in which healthy female volunteers were randomized to sertraline or placebo. The study terminated early, with all those receiving sertraline discontinuing because of problems in the domain of agitation and apprehension.

This study had come to my attention owing to an involvement in a medico-legal case, *Miller v. Pfizer*. Matthew Miller was a 13-year-old boy who, following a house move, had become disruptive at his new school and had been assessed for possible nervous problems. There were suggestions that he might be mildly depressed. He was given sertraline, and a week later he hanged himself.

Ten years before my involvement in the *Miller* case, shortly after fluoxetine and fluvoxamine had been launched on the British market, I had written up a pair of clinical cases in which two individuals had become suicidal within the first weeks of treatment with fluoxetine. The suicidality had cleared up on discontinuation of treatment but had re-emerged when re-challenged with a further antidepressant active on the serotonin system (Creaney, Murray, and Healy 1991). This had led to a review of SSRI-induced suicidality (Healy 1994), and that review in turn had triggered a series of medico-legal approaches. In all instances when consulted, I had offered the view that the SSRI in question, predominantly fluoxetine, had not caused the problems that the plaintiffs were claiming.

This picture changed in 1997, when I was approached on the case of William Forsyth, a man who after taking Prozac for 10 days had butchered his wife and then killed himself. In this instance the drug did seem to me to be involved. But whereas Lilly had settled a great number of other cases prior to this, this case went to trial, and in the process I became aware of an increasing number of documents and data from within Lilly and elsewhere that reinforced my views that SSRIs could cause problems. The *Forsyth* case led to involvement in the *Miller*, *Motus*, and *Tobin* cases. *Miller* and *Motus* involved sertraline and Pfizer, while *Tobin* involved paroxetine and SmithKline Beecham (now GlaxoSmithKline).

TORONTO

Towards the end of 1998, I had a first overture about a possible move from Britain to the Centre for Addiction and Mental Health (CAMH) in the University of Toronto (formerly the Clarke Institute). This led to interviews with the search panel in the course of 1999, and a formal university job offer, which in early 2000 I accepted. The position was as Professor of Psychiatry in the University of Toronto, and Head of the Mood and Anxiety Disorders Program within the CAMH. Aspects of the recruitment process and visa applications led to four visits to Toronto during the course of 1999 and 2000. In a series of lectures, I presented research on the history of the antidepressants (Healy 1997), as well as research indicating that Mental Health Services in general may be doing less well than is commonly portrayed (Healy et al. 2001). In the course of various meetings, I made no secret of my involvement in the SSRI controversies, on which I had several current publications (Healy 1999a; Healy, Langmaak, and Savage 1999; Healy and Savage 1998). My impression was that this involvement

indeed might have been attractive to some within the CAMH, who had concerns about the possible conflicts of interests set up by a growing receipt of research funds from pharmaceutical companies.

On a personal front, involvement in SSRI medico-legal issues made no difference to my willingness to undertake clinical trials of psychotropic agents or my preparedness to be a consultant to pharmaceutical companies or to lecture at company-sponsored symposia or in other venues. These involvements have continued through 2001. I prescribe SSRIs and had in fact been a particular advocate for sertraline in Wales, ensuring that it was listed as the SSRI of choice in the hospital formulary. The problems of possible suicide induction as I saw them were ones that could be handled with appropriate warnings and monitoring. I envisaged no problems in approaching companies for research sponsorship or research collaborations after taking up my post in Toronto.

In August 2000, I was invited to be a guest speaker at a meeting organized for the end of November 2000 to celebrate the 75th anniversary of the University Department and the 150th anniversary of the establishment of Clinical Services in Toronto. I agreed to talk on the topic of psychopharmacology and the government of the self (Healy 2001d). The talk in essence would give the outlines of a then-forthcoming book from Harvard University Press that overviewed the emergence of psychopharmacology, the development of the field, and prospects for the future (Healy 2001b). This seemed appropriate in the context of a meeting called "Looking Back, Looking Ahead." I had arranged to give the same lecture the following week at Cornell Medical School, as part of the Eric T. Carlsson Memorial Grand Rounds in the History of Medicine and the Richardson Research Seminar Series. Part of the lecture had been given previously at the invitation of AstraZeneca. The full lecture has subsequently been given in Paris, Minneapolis, Cambridge, and elsewhere.

On the day before the meeting in Toronto, I sat on an interview panel to appoint a neuropsychologist who would work with me on the Mood Disorders Program. I also was consulted about the decor of my office, as well as computing support, and I discussed moving expenses and associated issues with David Goldbloom, the Physician in Chief of the CAMH. I mentioned my SSRI medico-legal work to him, which he appeared to view as potential departmental funds. His only concern appeared to be to get me safely ensconced in the University of Toronto, even earlier than I had planned to get there. I was less than two weeks away from completing the last formalities in the visa process.

As is customary these days, the lecture in Toronto was rated for presentation and content by the audience, which was made up of over 200 people from across the board in the Mental Health Services. My lecture was rated highest for content. The same lecture was very warmly received at Cornell the following week, as it has been elsewhere since.

But in the hours following the lecture, I was told that David Goldbloom had

taken exception to some of the points that had been raised. The points that concerned him, I was told, were that I had claimed that Prozac could make people suicidal, that Lilly knew about it (a claim not made), and that we were now treating more patients than ever before (see Healy et al. 2001). I arranged to meet with Goldbloom following a celebratory meal that evening. He was apoplectic. There are only three points he told me that any one would ever remember from a lecture—and in this case the points they would remember were that Prozac makes people suicidal, that Lilly knew about it, and that high-dose antipsychotics can cause brain damage. A further charge that appeared later was that I had claimed that very large proportions of the clinical literature were now ghostwritten.

The following day I left for New York. My schedule involved spending three days in Pfizer's New York archives, where I wanted to look at their unpublished healthy volunteer studies with sertraline, before lecturing at Cornell.

Following the lecture at Cornell, there was also a meal. At this, the Dean of the Medical School, Bob Michels, asked what had happened in Toronto. Astonished at the enquiry, I outlined the story above. Michels, however, knew more than I did. Retrospectively, he appears to have known that the CAMH had taken the step to rescind my job offer as they saw it—breach their contract with me, as I was later to see it. How had he known?

I still do not know the answer to this, but it turned out that one of the lecturers at the Toronto meeting, Dr. Charles Nemeroff, attending the American Foundation for Suicide Prevention council meetings in New York the day after the Toronto meeting, had volubly raised the issues of Healy and his views on SSRIs. It later transpired that his lawyer, Nina Gussack, who has represented Lilly on occasions, made it clear that Dr. Nemeroff had been approached during the day previously when he was in Toronto, that he had made his views on Healy clear at that point, and that he had been left with the impression that choices had been made there and then. I was later to find out by email that there apparently had also been at least one phone call to senior figures at Cornell in the days before I lectured there, making what appear to have been extraordinary claims and apparently suggesting the invitation be withdrawn.

Following the lecture at Cornell, I arrived home from New York to find an email waiting from David Goldbloom, saying that: "Essentially, we believe that it is not a good fit between you and the role as leader of an academic program in mood and anxiety disorders at the Centre . . . we do not feel your approach is compatible with the goals for development of the academic and clinical resource that we have. This view was solidified by your recent appearance at the Centre in the context of an academic lecture."

CHEYENNE

When it came to considering the ramifications of these events with the University of Toronto and their potential impact on my future career, there was a

pressing issue to be addressed. I was at this point involved in a case, *Tobin v. SmithKline Beecham*, which was due in court in Cheyenne, Wyoming, in May 2001. I could envisage a situation where my first question on the witness stand would be about being sacked from the University of Toronto. Where my first instincts would probably be in line with almost everybody else's instincts in a situation like this, namely to lie low, it seemed I had little option but to do something.

On 15 February, I wrote to the Chair of the Ethics Committee at the CAMH. I outlined that there were a number of issues at play here, and that in all probability neither the CAMH, the university, nor I knew the full dimensions of what was happening. For instance, I pointed out that in March 2000 there had been a special issue on Prozac brought out by the *Hastings Center Report*, probably the premier bioethical journal in the world. In this, three philosophers with an interest in psychiatry, Carl Elliott, James Edwards, and David DeGrazia, along with Peter Kramer, a psychiatrist with an interest in philosophy, had written a series of elegant articles on the use of Prozac and the relationship between depression and alienation (DeGrazia 2000; Edwards 2000; Elliott 2000; Kramer 2000).

My piece, called "Good Science or Good Business," was more a "wake up and smell the coffee" piece—Prozac was about money (Healy 2000b). The antidepressants and depression were almost unknown outside of mainstream psychiatry 20 years previously, but we were now apparently in an Age of Depression (Healy 1999b). The antidepressant market had grown 800 percent by value in the 1990s, and by 2000 had become a $10 billion market. Based on other work, this article made the points that we were treating more people than ever before, that Prozac could make people suicidal, and that an increasing proportion of the therapeutics literature was ghostwritten.

It turned out that Lilly was one of the biggest private funders of the Hastings Center, and following this article they withdrew their support. The Hastings Center, uncertain what to do, had my article re-reviewed. One of these re-reviews said that essentially the only mistake I had made was in not going far enough in spelling out how much of the psychopharmacology literature was ghostwritten, how many of the clinical trials being run with psychotropic compounds ended up sealed, and how much of the research was market-oriented rather than designed to answer scientific questions. The Hastings Center did not apologize to Lilly.

The CAMH had received a great deal of money from Lilly, SmithKline Beecham, and other companies. In the year previously, CBC television was later to report, around 50 percent of the Mood Disorders Program's research money had come from pharmaceutical company sources. Had this played a part in the decision? Given that the points of concern in my lecture were similar to the points made in the Hastings Center article, which had appeared almost a year before, there was a set of background issues against which the CAMH decision to breach my contract was likely to be judged in the wider academic domain. Surely this provided grounds to talk before the situation got out of hand.

My hope was that if the CAMH were better appraised of the dimensions of the problem, key figures in both the CAMH and the university would be interested to meet and try to find some solution. I was due to speak in April at a meeting in Toronto and we could have met then. But far from being interested in meeting, the Chair of the Ethics Committee didn't answer my February letter. It was answered by the Chair of the Board of Trustees in March—dismissively.

I turned to the Canadian Association for University Teachers (CAUT), who agreed immediately to assist me and wrote to the President of the University of Toronto expressing concerns. The response from the President to the CAUT was dismissive. In April the issue began to run in the media in both Canada and the United Kingdom.

In the *Tobin* case, which was rapidly getting closer, it seemed quite possible that Dr. Nemeroff or others who had been present at the American Foundation of Suicide Prevention meeting might be witnesses. This raised the possibility that my position in the University of Toronto would have become a significant factor in the case. SmithKline Beecham applied for and was granted a gag order to prohibit any mention of my conflict with the University in the course of the trial or in the media in the weeks prior to the trial.

The *Tobin* case began at the end of May. Donald Schell was a man with a history of several relatively brief episodes of depression. He had a prior history of an adverse response to Prozac in 1990. He had then subsequently been put on Paxil by another physician in 1998, and 48 hours later had murdered his wife, along with his daughter and granddaughter, who were staying with him for a few days, before killing himself. His surviving son-in-law, Tim Tobin, took out a case for wrongful death against SmithKline Beecham.

As part of my background research for this case, I had been given access to SmithKline Beecham's paroxetine healthy volunteer archive. It was clear from this that paroxetine caused agitation in around 25 percent of takers, that it did so in a dose-dependent way and on a challenge-rechallenge basis, and that there had been a suicide in the program. It also caused physical dependence in one study in around 85 percent of subjects (Healy 2001c).

This evidence of dependence was interesting in the light of SmithKline Beecham's license to claim their drug was useful for the prophylaxis of depression. This license was based on studies that re-randomized patients to placebo and interpreted the subsequent problems of those re-randomized to placebo as new illness episodes (Montgomery and Dunbar 1993).

The *Tobin* case raised questions about how much of a company's defense in these SSRI cases depended on ghostwritten, or company-only authored publications, or how often medical testimony was based on tabulated figures provided to an expert rather than on the raw data. In the course of the proceedings, it became clear that key studies had been terminated early, with their results left unpublished. It also became clear that despite a backdrop that gave serious

grounds for concern, there had been a failure to test paroxetine or other SSRIs for the induction of possible suicidality.

On 6 June, the court found against SmithKline Beecham and awarded damages of $6.4 million. This may be the first verdict against a pharmaceutical company for a psychiatric side-effect of a psychotropic drug.

BEYOND CHEYENNE

Before the University of Toronto breached my contract, it had a track record in conflict-of-interest cases. Some years before, when Nancy Olivieri, a hematologist at Toronto's Hospital for Sick Children, had raised the hazards of deferiprone, many in the international academic community were dismayed that she ended up in a three-year struggle to hold on to her job in the University of Toronto. While these issues may have achieved greatest salience in Toronto, there is a growing concern about conflict of interest in the therapeutic domain.

If a drug produces death in one taker per thousand, this might seem like an acceptable trade-off to patients, therapists, regulators, and others. But if that same drug gets taken by 50 to 100 million people, as has happened with the SSRIs, the outcome will be over 50,000 deaths. This is the public health multiplier, which can convert a relatively infrequent problem into a major public health issue. When I talk for or take consultancies with pharmaceutical companies, I am inevitably biased. The hope is that any of us who speak on company platforms will be biased only slightly. But be that bias ever so slight, if it is applied across all medical departments in all North American and European universities, the risk is that a medico-pharmaceutical multiplier will convert a slight bias into a real threat to the well-being of science.

Allied to this problem is the power of pharmaceutical companies to counter criticism. Consider the following: in April 2000, Joseph Glenmullen's *Prozac Backlash* was published. On publication a variety of media outlets, such as the *Boston Globe* and *Newsday*, received an unsolicited set of reviews of the book from senior figures in U.S. psychiatry, such as Jerrold Rosenbaum and David Dunner, as well as a number of more junior figures. *Newsday* received a set of reviews with a covering letter from Robert Schwadron of Chamberlain Communications, who had been handling public relations for Lilly in New York, offering to arrange further "independent" interviews for them.

When journalists have researched my concerns about SSRIs or my breach of contract, they have been invited to contact some of the same or similar figures to get an "independent view." None of these professors of psychiatry are paid for reviewing *Prozac Backlash* or taking calls about me—but they often have consultancies with, have conducted clinical trials for, own shares in, or are speakers for the companies.

The view these experts have offered in my case has had a certain consistency.

In early 2000, for instance, when ABC produced a program on the issue of SSRIs and suicide, it was put to the producers that Healy's study in which healthy volunteers became suicidal on Zoloft was uncontrolled, that it was undertaken on his employees, that it gave an impossibly high incidence of suicidality, and that the results were submitted to an obscure journal. Similar criticisms were made to journalists investigating the post-Toronto issues. Before these points were made, Pfizer and all other SSRI companies had available to them prior sworn testimony from me that the study was not conducted on employees of mine, that it was controlled with another antidepressant, and that our results were furthermore consistent with unpublished findings that Pfizer and the other companies had on file. The initial reports of suicidality had been peer-reviewed, and the main body of the study is in press in a prestigious journal (Tranter et al. in press).

In addition to having to cope with companies or other clinicians playing fast and loose with the details of a study, a string of reports came back to me concerning the supposed "real" reasons why Healy was let go. Many of these reports were libelous. This too forms a pattern. Several witnesses who had testified in cases involving SSRIs and suicidality, such as Martin Teicher and Peter Breggin, had various aspects of their private life dragged into the legal arena in a manner that is almost certain to have deterred many others from getting involved in these cases. In addition to her difficulties with the University of Toronto, Nancy Olivieri became subject to hate mail, which it transpired was directed at her by senior clinical colleagues (Birmingham 2001). When Ian Oswald, a psychopharmacologist in the United Kingdom, tried to raise the hazards of the hypnotic triazolam, he became subject to a libel action by Upjohn.

These examples would all appear to point toward an effort to control both medico-legal and more general debate on matters of concern about drug therapies. The issues at stake are anything but local to Toronto or personal to me or Olivieri. The SSRI companies argue, for instance, that the evidence I have been putting forward regarding SSRI-induced suicidality is not evidence of cause and effect. They argue that clinical studies in which the problem appears in individuals on treatment, disappears when the treatment is discontinued, and reappears on the reinstitution of treatment—along with evidence for a dose-response relationship between SSRIs and agitation and, indeed, evidence of agitation and suicidality emerging in healthy volunteers—does not provide evidence for a causal link.

The companies argue that cause and effect can only be demonstrated in randomized controlled trials and epidemiological studies. Leaving to one side the fact that these latter studies have not been undertaken, this argument is intriguingly the mirror image of the tobacco company position, in which lawyers and scientists arguing on behalf of the tobacco corporations have argued that epidemiological studies do not provide evidence of cause and effect, and that what is required is challenge, de-challenge, and re-challenge relationships, as well as dose-response relationships showing the emergence of tumors in human lungs

under the influence of smoke. Curiously, these mirror-image arguments of the SSRI and tobacco companies are sometimes delivered by representatives from the same legal firms.

In the case of the SSRI issues, the problems for the community are even graver than they are in the case of the tobacco litigation, in that prescription-only status means that these drugs, unlike tobacco, are sold through physicians. Prescription-only arrangements were put in place in part in the belief that physicians would be better placed to bring attention to the hazards of therapies than patients would. But in practice, these arrangements also mean that pharmaceutical companies have been in a position to win the hearts and minds of physicians in a way that tobacco corporations have not been able to do. The experts on pharmacotherapies are the ones who speak on company platforms and who often become advocates for a new therapy, in a way that never happens with tobacco. One consequence of this is that the community effectively has had its experts body snatched from it. It is quite conceivable that companies could deliver adverse medical events with legal impunity in the near future, owing to the fact that experts are not prepared to testify against a company. In fact, in the case of the SSRIs, American legal firms have had to turn to someone like me in Britain to get an expert, owing to difficulties in getting an American expert.

There is a further, broader issue, in that the evidence being used against claimants in the SSRI cases is drawn from clinical trials that were never designed to establish whether the adverse events in question occur or not. Indeed, in many instances, the trials of the SSRIs have not recorded these adverse events when they happened, owing to a lack of boxes corresponding to the side effect in question. This lack of recorded data has then been used against claimants as evidence that the supposed problem doesn't happen. De facto, therefore, anyone participating in any company-sponsored clinical trial at present is putting all the rest of us in a state of legal jeopardy.

If the marketplace worked properly and brought competing compounds into the therapeutic arena at the same time, we might be able to depend on companies to ferret out the hazards of their competitors' compounds. But in practice, possibly because of current patenting arrangements, new agents come to the market in classes, and this means that none of the companies sponsoring any of these agents has any incentive to detect what may be class-based problems.

It might be expected that this interpretation of broad-based problems should lead to a response from pharmaceutical companies, but in fact it seems at least as likely to lead to anger from other clinicians, and for their response to be directed ad hominem rather than at the issues. This is surprising, in that prescription-only arrangements were put in place in part in the belief that therapists would be better able than the average patient to extract information from companies about the hazards of medications. Far from seeing it as their primary goal to be an advocate for the patient in this manner, however, some physicians seem to regard any interference with their ability to do therapy as likely to do more harm than good.

There is a public health argument that can be made—and has been made by the CAMH in my case. Raising awareness about a hazard like suicide on antidepressants could conceivably do more harm than good, by deterring people at risk of suicide from seeking treatment, and the greater good might therefore be better served by keeping quiet about the hazard. Against this background consider the following: a recent review of studies submitted to the FDA as part of license applications for five antidepressants licensed in the 1990s, two SSRIs (sertraline and paroxetine), two agents with other actions on the serotonin system (nefazodone and mirtazapine), and buproprion (Khan, Warner, and Brown 2000) produced figures of 27 suicides and 90 suicide attempts on new antidepressants from 12,897 patients, compared to two suicides and 14 suicide attempts in 3,079 patients randomized to placebo. In fact the two suicides apparently on placebo, as well as five suicide attempts, occurred during the withdrawal phase from other treatments rather than while on placebo, leaving no suicides on placebo and nine suicide attempts (Brecher 1991; Lee 1990/91). These revised figures give a statistically significant increase in suicides and suicide attempts on active agents compared to placebo. These figures also contain a statistically significant excess of suicides on paroxetine compared to placebo.

These figures take the force out of any public health criticism of my position. But beyond that they are worrying. In the face of this overall increase in suicidal acts, the best evidence for the continued use of newer agents, including the SSRIs, lies paradoxically in the healthy volunteer study we had conducted (Tranter et al. in press). This and other studies indicate that while some individuals may not suit SSRIs, others can be expected to respond very well.

Whether the hostility from individual clinicians stems from public health concerns or not is unclear. But this hostility seems to be mirrored at the institutional level. In both my case and Olivieri's, the CAMH and Toronto Sick Kids respectively went into a corporate mode of news management that would have impressed any pharmaceutical company. All communication in my case was effectively directed through one person, Paul Garfinkel, chief executive officer of the CAMH, who intriguingly had written an article on conflict of interest just before my case blew up (Garfinkel 2001).

In both instances, the University of Toronto's strategy appeared to be the same: to maintain a distance from what they portray as the somewhat cowboy practices that go on in teaching hospitals affiliated to the University. This strategy seems to breach the articles of association between the University and its affiliated hospitals (Perrin 2001). While there has historically been some distance between medical schools and their associated universities, as medicine increasingly moves toward an application of biological sciences, this strategy must become of increasing concern to scientists for whom freedom of speech has been a traditional value in a way that has not perhaps been the case within the medical "guild."

Over 50 years since the end of World War II, we have moved from a situation

where clinicians devised new scientific evaluative methods for the new therapies that came into medicine analyzed the results from trials, and wrote up the outcomes, to a situation in which companies hire clinicians to carry out off-the-peg protocols, the results of which are analyzed in-house and written up in-house or by communication agencies (Healy 2001b). This theme had been close to the heart of my Toronto lecture. Many trials now remain unpublished and in the process we have reached a point where the greatest determinant of the outcome of a published study is the identity of its sponsor (Freemantle et al. 2000; Gilbody and Song 2000). Part of my awareness of these issues stemmed from the fact that on several occasions after agreeing to take part in symposia, I had had "my" article sent to me. In one instance when I opted to write my own article, arrangements were made to have another name in the field "author" the ghosted article, leaving two articles full of Healy references sitting side-by-side in the same journal. An unpublished review I had undertaken in 1997 of Medline-listed review articles on the treatment of depression against a background of physical illness had revealed that 50 percent of them had been published in journal supplements or by company authors. This provides the basis for an estimate that up to 50 percent of the pharmacotherapeutic literature, at least in psychiatry, may be ghostwritten (Healy 2001d).

These problems seem likely to get worse as venture capital becomes increasingly involved in research. It must be of concern to scientists and not just physicians, in that increasingly scientific research only sees the light of day if it coincides with market interests. More subtly, good research may be published but effectively buried, if it is not selected for promulgation based on the support it offers for products that make it to the marketplace. Concerns such as these led 27 of the most senior figures in world psychopharmacology, including two Nobel Prize winners, and former presidents of the American Psychiatric Association and the American College of Neuropsychopharmacology, to sign a letter on 4 September to the University of Toronto, protesting against the violation of academic freedom involved in the breach of my contract. Some did not agree with my position on SSRIs and suicide, but none thought that I had addressed the issues in other than a scientific manner.

The growing concerns in the therapeutic and related arenas have reached something of a focus around the patenting of human tissues and sequences from the human genome, but the developments outlined here suggest that patenting may have become a symbol for wider concerns, involving non-publication of trial results, ghostwriting, and other changes in the traditional practice of science. In the face of non-publication of clinical trial data, the editors of the most distinguished medical journals have taken to encouraging a full disclosure of trial results. The implication is that this will make everything scientific. But the full disclosure of trial results would only restore us to a situation of acceptable business practice. To become scientific, we have to ask and engage with scientific questions, rather than simply publish the results of market-oriented technical studies.

Toronto provided me with a crash course in legal areas I had never expected to get involved in. One of the lessons is that contract law generally trumps everything—whether it will in my case remains to be seen. My situation led to a legal action against the University on 24 September for breach of contract, libel, and a first-ever action for violation of academic freedom.

These actions may point toward one protection that both healthcare consumers and scientists can have in the new marketplace. Since it is in fact our voluntary participation in studies as patients and researchers that underpins all market capitalization in the healthcare arena, it may be time for participants in clinical trials—or perhaps in all medical procedures—to transform informed consent forms into contracts that would specify that any use of data resulting from the use of "my body" needs to be agreed before such use takes place. Such a contract could lay the basis for many things, including even remuneration in certain cases. But of perhaps greatest importance, it would provide a legal means to enforce disclosure of data and information, without which neither science nor freedom can thrive.

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