10. The Plots Thicken

Shortly after I wrote up the healthy volunteer study, the cases of Matthew Miller, Viktor Motus, and Donald Schell triggered access to Pfizer and SmithKline's healthy volunteer studies. Working through Pfizer's internal documents in the Miller case, Andy Vickery came across the study Ian Hindmarch had done in the early 1980s, which Hindmarch himself had outlined for me some years before. His results were even more startling than our study:

> [O]f 12.. healthy volunteers entered into this study, five in the first week of the study were randomized to Zoloft, and seven to placebo. And of the five randomized to Zoloft, all dropped out in the course of the first week for what appears to have been fairly severe anxiety or agitation.[i]

When I was deposed in the Miller case at the end of March 2000, Pfizer's lawyers stated that details of this study had been sent to the FDA.[ii] I had just sent the details of our study to both the FDA[iii] and the MCA in Britain. The regulators now had more convincing evidence in favour of a license application for Zoloft for the production of agitation than they possessed when they licensed Zoloft for the treatment of depression. My covering letter to both sets of regulators asked whether they had anything comparable on file. I never got a reply from the FDA. But a fascinating correspondence began with the MCA which showed they simply did not know the contents of the healthy volunteer studies on these drugs.[iv]

For example, the regulators did not know that in the 1980s both Zoloft and Paxil were shown to produce dose-dependent agitation and apprehension in healthy volunteers. These studies were often conducted on company personnel and supervised by clinicians specialized in ENT or gastro-intestinal medicine rather than psychiatry. Nonetheless, rates of agitation in up to a quarter of volunteers were noted. Many subjects dropped out on the SSRI, and there was even one suicide. In one study on Paxil, after only a few weeks

on the drug, a significant dependence syndrome was visible in up to 85% of healthy volunteers upon withdrawal.[v]

Suicide in Children—The Miller Case

In the early 1990s the striking manic-depressive illness of someone like Kay Jamison, which began in her teenage years, and the real risk of suicide such an illness poses, had stimulated various campaigns, such as DART and Defeat Depression, hoping to increase recognition of such conditions and to lower national suicide rates. This was a legitimate, even a noble cause. Manic-depressive illness and some forms of melancholia or endogenous depression may begin in childhood or adolescence. But at that age these disorders are so rare that no clinical trial has ever been conducted of any antidepressant in these patient groups—there simply aren't enough patients around. Children and adolescents nevertheless experience much unhappiness and distress. Until the 1990s, received wisdom held that for the most part, childhood or adolescent distress was not the same thing as manic-depression or endogenous depression.

That view began to change in the 1990s. In America and elsewhere, children and adolescents were given psychotropic drugs with increasing frequency. In some cases this might be entirely sensible: for example, classic obsessive-compulsive disorder (OCD) can begin as early as the age of three. SSRIs can make a difference in many cases of OCD in adults; there is no reason to believe OCD in children wouldn't also respond to treatment, even though the drugs had not been tested in these age groups. Faced with a convulsing child, few clinicians would hesitate to give anticonvulsants although most anticonvulsants have not been tested in children.[vi] A prescription for lithium or even ECT can similarly be justified for a teenager with manic-depressive illness.

Serious depression is extremely rare in childhood, but there are enough distressed and unhappy children to conduct trials of antidepressants in

childhood and adolescent age groups. These began in the 1980s and early 1990s. Results uniformly failed to provide any evidence the drugs worked. Some pharmacotherapists argued that these age groups didn't respond to tricyclic antidepressants but the new SSRIs might offer an answer. In fact the SSRIs fared little better, prompting Seymour and Rhonda Fisher to ask, in a 1996 review in the *Journal of Nervous and Mental Disease*, whether the usual rules of science were somehow being suspended. The trial results were uniformly negative, they pointed out, yet clinicians were prescribing increasing amounts of antidepressants to children.[vii]

Clinicians saw children and adolescents respond to Prozac and other SSRIs. The confounding factor here is that clinical trials of antidepressants in distressed children show extremely high placebo response rates. These responses might simply have been because someone was paying attention to these children. High placebo response rates mean it is very difficult for *any* other treatment to do better. When I convened the British Association for Psychopharmacology consensus meeting on prescribing for children and adolescents in early 1997, however, I was assured that a new trial in press, conducted by Graham Emslie, would show Prozac really did work.[viii]

In brief, Emslie and colleagues first excluded subjects showing a placebo response. This left them with a group of subjects randomized to Prozac or placebo. In that pool of subjects Prozac did do better than placebo, but not dramatically better. Critics of pharmacotherapy argue placebo washouts produce an extremely artificial situation. But this design does demonstrate that Prozac does something. An effect suspected by many was in fact demonstrated in some patients, thus providing some legitimacy for prescribing an SSRI to children or adolescents. But the finding does not legitimize widespread prescribing in this age group. Indeed, this trial demonstrated that many children—perhaps a majority—did no better on Prozac than they would have done simply seeing a sympathetic clinician.

Prescriptions boomed nonetheless. *Newsweek* and other periodicals featured the rising tide of Ritalin prescriptions in the mid-1990s. Whatever the rights

and wrongs of giving drugs to children, there was a large body of evidence that stimulants could improve many children's lives. By the end of the decade, *US News and World Report* and other periodicals had moved on from Ritalin to questioning what was going on in the case of Prozac and the other SSRIs.[ix] The *US News and World Report* article featured Matthew Miller.

Thirteen-year-old Matthew was a restless kid experiencing difficulties after moving to a new school. Concerned about his behaviour, teachers administered a set of questionnaires and tests on which his scores fell marginally outside the normal range. His parents agreed to take Matthew to a psychiatrist. In June 1997 he saw Douglas Geenens,[x] who was also a consultant for and speaker for Pfizer. Geenens considered either a possible depressive disorder or ADHD. Matthew's depression, if it was present, was mild and non-specific in nature. There was no indication that this was the onset of a manic-depressive disorder. Hospitalization was not considered. Had the Millers' HMO coverage provided for psychotherapy, this would probably have been the next step. Instead, after a second consultation in July, a prescription for Zoloft was arranged. The initial pills came from a sample left with Dr. Geenens by his local Pfizer representative. He warned the Millers that Matthew might experience some nausea and insomnia.

During the next week, Matthew looked normal to his parents. His grandmother noted at one point over a meal that he was fidgety, "jumping out of his skin."[xi] A questionnaire filled out by Dr. Geenens had noted that Matthew had ideas he might kill himself but would not do so. This changed. He met two girls to whom he confided he was thinking of burning down his parents' house.[xii] In the early hours of the morning, a week after going on Zoloft, Matthew Miller hanged himself in the closet next door to his parents' bedroom.

Rather than settle, as it had done in the case of Bryn Hartmann, who killed her husband and then herself after 10 days on Zoloft,[xiii] Pfizer fought the Miller case. It argued suicide is the second commonest cause of death in 13-year-old males. It is—but only because 13-year-olds don't often die. There had been only 61 suicides among 155,000 13-year males in 1997. One expert,

Parke Dietz, argued that because Mathew Miller had not hanged himself from a height, this might be a case of autoerotic asphyxiation gone wrong.[xiv]

During the pretrial process I was able to examine Pfizer's clinical trial database involving over 8,000 patients as of December 1991, just before Zoloft's launch in America. My analysis suggested patients on Zoloft were almost twice as likely as patients on placebo to go on to suicidal acts.[xv] Pfizer, using the dubious methodological step of calculating rates of suicidal acts in terms of patient exposure years, found the relative risk for suicidality on Zoloft to be almost identical to placebo.

Another document reported that six children and adolescents had become suicidal on Zoloft in the course of studies for depression and OCD. There were four suicidal acts in 44 depressed children—a rate ten times higher than that found in adults. In the case of one eight-year-old boy, the investigator blamed Zoloft.[xvi] It was in this case that Wilma Harrison had tried to blame the disease and not the drug (see chapter 8), even though Pfizer monitors had agreed that the activating effects of Zoloft had likely led to the child's suicidality.[xvii] Despite this report filed by the company, and evidence of a high rate of suicidality on other SSRIs in this age group, the FDA did nothing.[xviii]

Old stories came back to light in the course of the Miller case. In 1994 Seymour Fisher and colleagues in Texas surveyed behavioural effects of Zoloft and Prozac and found an equivalent rate of emergent suicidality on Zoloft. (A few years previously they had found a much lower rate on trazodone compared to Prozac.) Fisher posted details on the Internet of how Pfizer attempted to block publication of his study and, when that failed, how the company sought to diminish its impact.[xix]

I was deposed in the Miller case in Boston in March 2000. Our healthy volunteer study comparing reboxetine and Zoloft was scrutinized. This led to an interesting media portrayal of the study in the following weeks, one completely at odds with all the material given to Pfizer's lawyers. It was claimed that all subjects were my employees.[xx] Only one of the 19 had been

on my staff—unless you argued that being paid inconvenience money made them my employees. It was claimed I had not examined any of the volunteers medically or psychiatrically. This was true—because it would have been inappropriate for me to do the examinations. Other medical staff examined them. Finally, it was claimed Max had a significant alcohol disorder, when in fact she took two glasses of wine per week on average and had never taken more. But how could I rebut any of these assertions? This was the start of increasingly personal attacks on me; briefs for court actions and feedback from journalists characterized me as a zealot who said one thing for money in court or to the media and quite different things in scientific forums.

The Prozac Patent

The Miller case fed directly into the Prozac story. On 25th February 2000 a court in Milford, Connecticut acquitted Christopher DeAngelo of robbing a bank because he was on Prozac at the time.[xxi] Another court in Britain acquitted a man who had been on Prozac on an assault charge.[xxii] The Forsyth appeal was also pending.

These interconnected stories led the *Indianapolis Star* to ask how Lilly had managed the legal time bomb of Prozac in the mid-1990s. The paper ran a story on how the MDL cases involving Paul Smith's alleged breach of fiduciary obligations to his colleagues were been held up in Indiana for several years. Mitch Daniels, a spokesman for Lilly, commented that it was an illuminating spectacle to see sharks turn on each other. Daniels, a former top aide to Ronald Reagan and president of the Hudson Institute and later a member of George W. Bush's cabinet, characterized the over $50 million in known Lilly settlement payments over Prozac cases as "relatively insignificant."[xxiii] Had Lilly been forced to withdraw the drug or substantially alter the labeling, the company might have faced $2–3 billion in settlement claims. Lilly's main loss, if any, came from whatever dip in sales the controversy might have caused.

After the publication in April 2000 of Joseph Glenmullen's *Prozac Backlash,*[xxiv] ABC's "20 20" approached Martin Teicher, but were puzzled by his apparent lack of commitment either pro- or anti-Prozac. They found Teicher was now engaged in what seemed to be a study for Lilly of a "new" Prozac.

Celexa and Prozac have structures that mean the parent molecule can come in an original and a mirror-image form (called isomers). It is often difficult to separate the two isomers in early industrial production, and companies therefore develop a "mixture" of the two. The side effects of these mirror images can be quite different, enabling a company to apply for a patent on the more effective or better tolerated of the two mirror images—if they can separate them.

In 1991 the Massachusetts-based company Sepracor isolated the isomers of Prozac—S-fluoxetine and R-fluoxetine (or dexfluoxetine/ dextra-fluoxetine)—and needed someone to help determine their potential. Teicher had come into psychiatry from animal pharmacology. After describing the hazards of Prozac in 1990, he returned to animal research in an effort to model Prozac-induced akathisia.[xxv] This made him the obvious person to establish the behavioural profile of Sepracor's new drugs. His work suggested R-fluoxetine lacked the activating profile of S-fluoxetine. Sepracor took out a patent for R-fluoxetine in 1995[xxvi] which bound them, Teicher, and McLean Hospital together. In 1998, Lilly bought the marketing rights to the patent in a deal that potentially offered Sepracor up to $100 million per annum.[xxvii]

After early hype, *Prozac Backlash* might have died a quiet death. ABC stalled on broadcasting their program. But then the Boston *Globe* found itself in receipt of a number of unsolicited critiques of the book which were also sent to media outlets such as *Newsday* in New York. These included a commentary from John Greist of the University of Wisconsin, a witness for Lilly in the Wesbecker case. Another was by Graham Emslie, whose study of Prozac in children we have noted earlier. A third came from David Dunner, a clinical triallist for Lilly and member of the 1991 FDA panel on Prozac. A fourth came from Harvey Ruben of Yale. All followed a standard line about the

devastating disease that was depression, the weight of research behind Prozac, and the patients who would commit suicide because they had been scared off treatment.

In one commentary Tony Rothschild claimed to be

> disheartened that Dr. Glenmullen bolsters many of his arguments and proves his hypotheses by borrowing liberally from others' work including my own....at no point did Dr. Glenmullen consult me directly to question my studies, two of which he conveniently uses to prove his argument.

I had tried unsuccessfully to contact Rothschild to talk about just this. It was well known that Carol Locke, the senior author on the Rothschild and Locke publication, stood by her view that the study pointed toward a causal relationship between Prozac and suicidality. Jerrold Rosenbaum from Massachusetts General, who apparently owned up to not having read the entire book, was also quoted in the material sent to the *Globe*. When approached by the *Globe* and asked about his consultancy with Lilly, he claimed that pretty well every senior person in the world of psychopharmacology had consultancies with a range of different companies—that in fact it was impossible to function in this world without these links.[xxviii]

The commentaries sent to *Newsday* in New York included a delicious covering letter from Robert Schwadron of Chamberlain Communications Group:[xxix]

> The book preys on the fear of people with clinical depression, and may prompt some people to abandon their medication and seek medically unproven alternatives for a debilitating disease with potentially life-threatening consequences.. If we can offer you any information, or some balance to a story you may be planning, we would be more than happy to oblige. We can arrange for interviews with spokespeople from Eli Lilly and Company, as well as with independent researchers from the medical community.[xxx]

The *Globe* materials came from Rasky Baerlein, a PR group working for Lilly. This prompted Leah Garnett to investigate. Garnett was an assistant health editor who had come to the *Globe* a few months before from the *Harvard Health Letter*. She was on her way to a freelance career and was clearing her desk as the story came to a head. She wanted something new on Prozac that Lilly would find difficult to portray as selected documents stemming from plaintiffs' attorneys. The answer came to her in the middle of the night: she could just go to a government Web site and use the search terms Teicher and Sepracor to look at the patent for the new form of Prozac. What she found led to a headline feature on the front page of the *Globe* days after she left the newspaper.[xxxi] The new patent stated that "Furthermore, fluoxetine produces a state of inner restlessness (akathisia), which is one of its more significant side effects."[xxxii] "The adverse affects which are decreased by administering the R(-) isomer of fluoxetine include but are not limited to headaches, nervousness, anxiety, insomnia, inner restlessness (akathisia) suicidal thoughts and self mutilation."[xxxiii]

If the new "Prozac" ever reached the market it would presumably carry warnings that it could cause suicidal thoughts—even though it might be less likely to do so than the parent compound. Replying for Lilly in the Boston *Globe*, Gary Tollefson took a familiar tack, arguing that sufferers from the debilitating disease that was depression were being unwarrantedly stigmatized and the result of this would be that they would fail to seek treatment and lives would be lost. He claimed that the weight of scientific research made it abundantly clear that Prozac didn't cause any of the problems claimed for it.[xxxiv]

This opened up the possibility that groups like the Church of Scientology might use Lilly's own clinical trials and interpretations of their meaning to squash the new patent, on the basis that it did not contain a valid new development. Could Lilly deny the basis for patenting and still hold onto the patent? The possible ramifications were fascinating.

The patent on R-fluoxetine impacted on the legal game. One of the remaining Prozac cases was also one of the original cases, the one left in Nancy Zettler's files after the Wesbecker trial depleted her resources. It dated back to the August 1991 suicide of "Corky" Berman, a wealthy businessman from Chicago. Berman leapt from the 37th floor of the Carbon and Carbide Building, a striking art deco skyscraper on North Michigan Avenue in which Berman's psychologist kept his office.[xxxv] Berman had ended up in a style of therapy that became common with managed care—he was seeing a psychologist for "therapy" and a pharmacologist (a psychiatrist[xxxvi]) for his prescriptions. On a 10mg dose of Prozac, he appeared to have a range of side effects for which he was prescribed antidotes, including trazodone. Not unlike some of our healthy volunteers, he also underwent a change of personality. His psychologist, who had no knowledge about the possibility that Prozac might cause this, commented extensively on this change of personality. Two weeks after his dose of Prozac was bumped up dramatically, and a few hours after visiting his psychologist—who saw him as apparently normal and definitely not suicidal—Berman jumped to his death.[xxxvii]

Shortly after Berman's widow took legal action, the prescribing psychiatrist, David McNeil, was persuaded to switch insurers and avail himself of an indemnification package then offered by Lilly to American psychiatrists.[xxxviii] The Berman case brings out the hazards in this arrangement, under which McNeil had little option but to take the advice of his new lawyers, who were also involved in Lilly's defense. What if the best company defense were to hang McNeil out to dry? He had prescribed the sedative trazodone to counteract Prozac side effects. How would he justify what he had done? *Where is the evidence that you should do this, Doctor? Did Eli Lilly ever tell you this would be a good idea?*

While I was being deposed in the Berman case in September, Andy Vickery was in Indianapolis, invited to discuss settlements in his outstanding cases. Baum, Hedlund and Vickery had filed an action on 8 June 2000 to supplement their appeal against the Forsyth verdict—claiming Lilly had perpetrated a fraud upon the court.[xxxix] The final deal between Lilly and Sepracor had been

struck in December of 1998. Three months later, in the course of the Forsyth trial, Lilly's patent lawyer Doug Norman had been present in the court. The plaintiff's appeal was based on a precedent set in a case against the Thompson Tool Co., a gun manufacturer, who had a video on file showing their gun firing accidentally when dropped. The relatives of a Mr. Pumphrey, who had been killed in just this manner, had appealed a "not guilty" verdict. The US Court of Appeals found Thompson had committed a fraud upon the court by failing to disclose the video. The new Forsyth action argued that failing to disclose the details of the patent amounted to a comparable fraud compounded by the presence of Lilly's patent attorney in the courtroom.

Vickery brought the R-fluoxetine patent into play in three outstanding cases. One involved Hugh Blowers, a 17-year-old Hawaiian who had hanged himself after a week on Prozac. Blowers had described symptoms of akathisia in an e-mail to a friend just before he killed himself, and his friends described a marked change in character. On his bedroom wall was a poster for Prozac and what it can do for you by normalizing your serotonin system—part of the reason Blowers pushed for a change of antidepressant. This case would take the doctor, McNeil or Neal, out of the equation. But then Vickery was asked to Indianapolis, where he settled the Blowers case.

Lilly believed the original Prozac patent held in the United States until December 2003. But in the week ending August 12th, an appellate court ruled competitors could begin to produce generic versions of fluoxetine from February 2001. Lilly's stock fell from a capitalization of $123 billion to $85 billion, making it vulnerable to takeover. Suddenly it had considerable incentive to settle all cases and to prepare to trash Prozac and the generic fluoxetines that would appear in 2001, making way for the new improved molecule they hoped to launch in 2003. Zettler and Vickery applied between them to depose Teicher, Beasley, and a series of Lilly lawyers, including Doug Norman, who had been present in Hawaii. Teicher, extraordinarily, would be deposed effectively as a Lilly scientist and Beasley was to be quizzed about the clinical trials program for the new compound, in particular about what steps were being taken to determine its suicide potential.

Then, in October 2000, Lilly shelved its development plans for R-fluoxetine (Zalutria). The investigation of the cardiac profile of dextra-fluoxetine suggested that the company might not get the new drug to market in time to forestall the competition.[xl] Sepracor's stock plummeted by 25%.[xli] Lilly was left with only duloxetine, a 1980s serotonin and norepinephrine reuptake inhibitor, in its antidepressant pipeline.[xlii]

I had first been approached about participating in a clinical trial of duloxetine in the early 1990s, before the company shelved the compound, as far as I knew because of bladder side effects. US psychopharmacologists dutifully praised the development that duloxetine constituted. But, probably unbeknownst to many of these experts, duloxetine had since been developed as a bladder stabilizer in many countries. Rebranding it as an antidepressant would raise interesting questions about duloxetine, not only among bladder specialists who knew nothing about its history as an antidepressant but also in the general public as well, who might well be mystified as to how a drug could be marketed for one condition in one country and an entirely different condition in others.

Conflicting Interests

While working on the appeal in the Forsyth case, Cindy Hall came across two memos that had gathered dust since 1994. In the first, a memo to the "I saved Prozac" team on 1st August, 1990, Leigh Thompson wrote:

> Today at PSC was LRL/Medical's finest hour. Dave Thompson and Gene Stap told me that it suddenly gave them a glimpse of how far medical has come and the vision that they knew (about global databases, super handling of ADE, proactive excellent relations with FDA, complex analyses and presentations made simple, DEN, GPT etc) but had never really had burned into their brains the elegance and mastery of the complexity!

> So many of us were not here for the Oraflex , Moxam, etc crises, that it is very hard to measure the progress over the last few months on so very very many fronts.
> When you battle the media and politicians, the ONLY thing that counts is the first word. The rebuttals are always on the last page and forgotten. You have to get out front and enlist your allies. The rapid flights to Boston to visit Teicher, the trips to FDA, the consultants coming in, the huge complex database, having so many large trials, the ability to quickly perform elegant analyses, DENs mastery of ADEs, have all come together in a significant effort.
> I'll try to give a global overview of our past (Oraflex and Moxam especially) and our present and our future (with Mobius, Scientology etc after us) tomorrow at DEN. Please pass on my congratulations and profound thanks to your spouses/friends for tolerating your extra work/pressure and to those colleagues whom I have left off the list of addressees in my rush to get out this note.
> I'd like to have some buttons or mementos of other kinds made with a logo along the lines of: "I saved Prozac." Suggestions please for design, memento and words—.[xliii]

The "I saved Prozac" effort in 1990 gave rise to the first version of the Beasley article. Laura Fludzinski was then head of the clinical research department in Lilly Europe. By the time she was deposed in the Wesbecker case, Smith and Zettler had focused on events in Germany, leaving the British story—and the 28th and final exhibit in Fludzinski's deposition—to languish. This exhibit included a memo dealing with a trip by Lilly's David Wheadon to Britain and Europe in August of 1990 to gauge opinions on the Teicher issues, and a set of reports from consultants for Lilly in response to an early draft of what later became the Beasley article.

Wheadon's memorandum mentioned that he hoped Allan Weinstein would be in good form when he saw the expense account. It also noted how some of those he had met were sure they could help Lilly with the problem—"Of

course, he had several ideas on how he could assist us with this!" The exclamation mark suggests bids for funding.

Wheadon's trip overlapped with my vacation in Galway, when Brian Leonard first asked me what I made of the Teicher paper (chapter 3). The next document up after Wheadon's memo was an assessment of the issues from Brian. What he wrote was much what I would have written at the time—skepticism that this was anything more than a periodic scare. He pointed to the lack of a neurobiological rationale for what was happening and the evidence from the fluvoxamine story that SSRIs might in fact be most useful in suicidal patients.

The mianserin story showed how a company needs a network of "friends" when a crisis blows up. Roger Pinder put together such a network for mianserin and Organon (see chapter 2); Brian Leonard was one of the figures involved. Responses from some of the others involved in the mianserin story were also in exhibit 28, including John Henry's. There was input from George Ashcroft, who had put forward the first serotonin hypothesis of depression. All these experts made exactly the points that might have been expected of them.

The revelation in Fludzinski came in another report. The Fludzinski exhibit noted in a covering letter that the key report came from someone whose views were likely to be particularly influential with regulators; the name was blacked out. It began:

> It comes as no surprise that the issue of suicidality and fluoxetine has surfaced as a problem for Lilly since I predicted it would some four or five years ago. … As you know there were questions about the agitation and stimulating properties attributed to fluoxetine and there were fears that this might increase suicidality…. I covered this issue in my expert report for the English and later in greater detail for the Dutch and German authorities.
>
> It was for this reason that I felt that Lilly would be wise to undertake a formal prospective study in this area. As you know I promised to examine

> the effects of fluoxetine or placebo in a group of multiple suicide attempters. At the time you will remember Lilly did not think this study had a high priority, which was reflected in the level of funding… I nevertheless regarded this as a sufficiently important issue to carry out the study using my own resources in my own time.[xliv]

Stuart Montgomery had begun a Prozac study in multiple suicide attempters. Lilly personnel were quizzed about this in 1994 depositions, but there was nothing in print. Later that year an article appeared titled "Lack of efficacy of fluoxetine in recurrent brief depression and suicidal attempts."[xlv] Despite the headline, the text claimed there was no evidence of an increased rate of suicidality and that this disproved Teicher's hypothesis. But the figures in the text belied the claim. The original study had been scaled back so that only 107 subjects from a planned sample of 150 had been recruited.[xlvi] Of those recruited, fewer than half completed the study with its randomization to Prozac or placebo. Of those completing, rates of suicide attempts were reported as the same in both the Prozac and placebo groups. But the fact that almost half the subjects dropped out made it impossible for the study to "disprove" Teicher's claim—almost by definition, all the Teicher cases would have dropped out early. Furthermore, although the paper didn't report the information, internal Lilly memos showed that on other measures placebo had done dramatically better than Prozac (p=0.006).[xlvii]

Montgomery subsequently undertook a similar study with Paxil in recurrent brief depression. Again as with Prozac the "preliminary" report, in another study that terminated early, showed no benefit for Paxil. But some critical details remained unpublished. At a psychopharmacology meeting in London in September 1999, David Baldwin, a former colleague of Montgomery's, reported that this group had shown a threefold higher rate of suicide attempts in those taking Paxil compared with those taking placebo[xlviii]—with a projected rate of 45 suicide attempts per year in the Paxil group and 12 per year in the placebo group.[xlix] SmithKline Beecham later defended this study by claiming the results were not statistically significant. But the main reason the results failed to reach statistical significance was that the study terminated early, after

only 36 patients had been recruited. The most serious suicide attempt involved a woman on Paxil who ended up with spinal injuries and later took an action against St. Mary's Hospital.[I]

These studies can be seen as a worthwhile effort to examine the benefits which a then new group of drugs, the SSRIs, might offer to a particularly difficult patient group, those who are highly suicidal. There turned out to be none. Even had SSRIs reduced suicidality in this high-risk group, this would not mean they couldn't at the same time induce suicidality in other individuals not at any risk of suicide. Indeed, a cynical argument would be that if one wanted to hide or manage an SSRI-induced suicidality problem, the very best group to pick was a high-risk group, where there was a much slimmer possibility that existing high rates of suicidal acts would increase.

SmithKline supported a further study in this patient group by Verkes *et al.*, who reported that Paxil reduced suicide rates compared to placebo. However, all but 19 out of 91 patients entered into the trial dropped out, making the entire study meaningless without at the very least a proper analysis of the reasons for dropout.[Ii]

When Lilly's expert went on to characterize the first draft of the Beasley report as "disappointing," it became clearer why Lilly might want the name blacked out. Lilly had failed to follow the approach taken by Jenny Wakelin, he said, which was to analyze the data from the more suicidal patients to see if they showed more benefit than other patients (see chapter 2). "Since these data [Wakelin's] are published it is reasonable to expect Lilly to have performed the same analysis and if it is not reported the assumption may be that fluoxetine has a less favourable effect."

He pointed out ongoing Lilly prospective studies which might shed light on the problem. The fact that there was no mention of results from these worried him. He noted Lilly had reported on a smaller number of trials than it had undertaken. "The decision to report on a smaller number of trials than the full data base may appear as evasive. In any event selective reporting on your

data requires adequate explanation, which is missing… Any suggestion that the full data base is not being examined will raise the thought in some minds that the data are potentially misleading."

In passing, he noted that in clinical trials suicidal ideation is not "systematically asked for and therefore is erratically collected and unreliable." He noted how poor item 3 on the Hamilton scale, the suicide item, was and how much better the suicide item in the Montgomery Àsberg Depression Rating Scale was.

He concluded:

> [T]he analysis is patchy and apparently not done on the full pool of blinded placebo and reference controlled data, which is available to the company. It is therefore suspect particularly since it contradicts already published data. The report refers in an offhand manner to the recent change in product labeling, to warn of suicidal ideation associated with fluoxetine. This conveys to me, and, I believe, most clinicians, that Lilly is convinced the data support the presence of a relationship between fluoxetine and the provocation of suicidal ideas. It is difficult to understand why this report provides no evidence to support this, and increases the feeling that other data not presented here must have helped persuade Lilly of the existence of a causal relationship.
>
> Overall the report is disappointing. The review is patchy and inadequate, the analyses undertaken are not in line with published data and do not give the numbers involved and provide limited data on the main question. The conclusions of the report contradict the recent change in product labeling and this adds to the impression that the question of whether fluoxetine provokes suicidal thoughts or not has not been properly considered.

Lilly had voluntarily inserted a reference to suicidal ideation and violent behaviours into a section on the labeling for post-introduction reports on the 29th of May 1990. This section reports on claims made after launch. But it is neither a warning nor a precaution nor an acknowledgment of possible causation.[lii] Looked at more cynically than their expert had done, it allowed

Lilly to claim that the wording was there for physicians to see. Jurors might, as a consequence, blame the physician rather than the company.

Many ambiguities about Prozac remain. In 1990 I found almost all my own, later criticisms of Lilly's position. This report cut to the heart of what ought to be done.

A few years later, in the case of Paxil, a very similar analysis to the Beasley analysis appears in publications from Stuart Montgomery,[liii] a former consultant to the British MCA, and again from Juan Lopez-Ibor in 1993,[liv] appearing in a two-page symposium supplement. These two articles and another by David Sheehan[lv] were the significant planks for SmithKline's medico-legal defense in the first case that came their way—the Tobin case. But, as we shall see, there were major mismatches between the data reported in these articles and the underlying raw data from SmithKline's clinical trials.

Nine years after the expert report for Lilly, at an ECNP meeting in London, Stuart Montgomery presented data from Pierre Fabre's meta-analysis showing that SSRIs were much more likely than milnacipran or tricyclic antidepressants to be associated with suicidality. At exactly the same time, Sarah Boseley was writing her *Guardian* article "Prozac: Can it Make You Kill?" When she contacted Lilly for comments, the company offered Montgomery as someone who might offer an "independent"comment.

When the difficulties posed by the patent of R-fluoxetine entered the public domain in May 2000, Lilly's response included the continued assertion that "Teicher's article was a series of anecdotal reports, and his suggestions of a 'possibility' of a causal relationship have been refuted by multiple large placebo controlled prospective and retrospective clinical studies that have demonstrated no increased risk of suicide associated with Prozac use."[lvi] However, when deposed as a Pfizer expert in the Miller case in 2000, Daniel Casey, who had chaired the FDA hearings in 1991, agreed that he was not aware of any prospective studies designed to test whether Prozac might induce suicidality.[lvii] John Mann, another Pfizer expert in the same case,

agreed.[lviii] As did Roger Lane of Pfizer, David Wheadon—once of Lilly but then of SmithKline—and Charles Beasley of Lilly, all during the course of 1999/2000.[lix]

Boss of Bosses

Charles Nemeroff, professor of psychiatry at Emory University in Atlanta and a senior figure in American psychopharmacology, gave the Annual Guest Lecture at the July 2000 British Association for Psychopharmacology meeting in Cambridge. At this meeting I presented the results from our healthy volunteer study in poster form. I did not attend the guest lecture, during which Nemeroff apparently mentioned disapproving of posters on drug studies in healthy volunteers.[lx] Others present at the lecture brought this to my attention, so I expected Nemeroff to visit me at the poster session. He did.

As I recall it, Nemeroff's opening gambit was that I was doing myself harm publishing such material.[lxi] Why? It was good clear-cut science, and other, unpublished studies backed up our findings. Nevertheless, I was warned, it would ruin my career to get involved in this. He said he had been approached on several occasions to participate in legal actions against me. This was a frightening prospect—as he phrased it.

Nemeroff claimed he had looked through the Lilly database at the time of the FDA hearings in 1991, and that in his opinion there was nothing there. He had in fact presented data on the company's behalf at the FDA hearings. I countered that I had also looked through Lilly's database and those of other companies, and in my opinion there *was* something there.

I pointed out that the clinical trials submitted to the FDA for new antidepressants showed an excess of suicidal acts on SSRIs compared to placebo. If the drugs reduced suicidality for some people, as both he and I believed, they must be causing it in others to account for the number of suicidal acts. This was brushed aside.

With the Hindmarch study in mind, I mentioned that our study was consistent with other healthy volunteer studies. Nemeroff immediately said that this other study involved a dose effect. This appeared to be a clear admission of a causal connection between the SSRI and emergent suicidality. Also, his reply, if I understood it correctly, would seem to suggest that he and probably other experts knew of the existence of either this or other studies.[lxii]

He went on to say that these were big companies in an $8 billion business, saying he himself had had problems with Pfizer some years back when the company managed to make life very difficult for him, for his research staff, and for others associated with him.

Did I want the consequences of creating a fuss about drugs like the SSRIs? American primary care practitioners would simply hear a message that there was a problem with these drugs and would stop prescribing them, and as a result more people would commit suicide. There would be a public health cost. Could I cope with this on my conscience? Could I cope with the string of flaky individuals who would bring cases my way—individuals who, both he and I knew, had difficulties that were not caused by the drugs?

What about his duty and mine, I asked, as prescribers of drugs available only on prescription, to warn other prescribers and patients of any hazards in order to make therapy as effective and safe as possible? He wouldn't engage on this point. Some would say it was immaterial what people like the two of us did—that these companies were so big they would simply roll over those who got in the way, as tobacco companies had done. They were answerable to their shareholders only, and profit was the bottom line.

But in addition to being a prescriber, under conflict-of-interest guidelines at other meetings, Nemeroff listed himself as a major equity shareholder in Lilly, Pfizer, SmithKline Beecham, Pharmacia and Forrest—all of the SSRI-producing companies.[lxiii] Some weeks later, I stumbled on a copy of a glossy new journal, filled with advertisements for pharmaceutical products, called

T.E.N.: The Economics of Neuroscience. The front cover was a portrait of Nemeroff captioned: “Boss of Bosses: Is the Brash and Controversial Charles Nemeroff the Most Powerful Man in Psychiatry?”[lxiv] There was no hint that the sideline or the profile inside was written ironically, or that the authors were aware of what the title and the text implied.

The possible great influence of a small group of people comes in Schatzberg and Nemeroff’s 1998 American Psychiatric Press *Textbook of Psychopharmacology.* Its chapter on SSRIs was written by Lilly’s Tollefson and Rosenbaum from Massachusetts General Hospital. This cited the Warshaw and Keller study as its only piece of evidence that Prozac does not cause suicide.[lxv] The chapter was later used by Pfizer in the Motus case as part of its basis for a statement of undisputed facts claiming that serotonin was low in depression, that SSRIs promote serotonergic function, and that the selectivity of SSRIs meant they were less prone to side effects than other antidepressants.[lxvi]

We have moved into a new world in which the Dean of Harvard Medical School publicly agonizes about the issue of conflict of interest. Harvard had previously set a ceiling of $10,000 support from outside interests but, alarmed that they might be losing senior figures to other universities, had decided to review their policy. In this new world, what duty of care or responsibility to the community do academics have? With duties as shareholders come opportunities to have an input into company policy in a manner not available to the ivory-towered academics of yesteryear. Individuals as shareholders have access to the right connections to do great good. George Bush previously sat on the Board of Lilly. But in order to do the right thing, Bush or others like him need a proper assessment of the situation. If the experts conclude that there is no problem, there is little that Bush or anyone else can do.

The Prozac story implied a very real calculus for senior figures in American psychopharmacology who, as shareholders, were perfectly placed to force a debate on major issues in public and academic forums. Teicher claims that

some of these figures had attempted to block his first efforts to raise the issue, offering essentially similar arguments to those with which I was now being confronted.[lxvii] The “advice” in my case could be construed as concern for my welfare, yet if followed it could shut down debate. But whatever was going on, who gave either Lilly shareholders or me the right to settle the matters of public importance involved in the Prozac case?

The Fludzinski exhibit indicates that the role of certain players goes beyond their duties as shareholders. Some of these experts are also advisors to regulatory bodies. Given the information that was published and which MCA knew about, it is hard to understand how Prozac could have remained on the British market without warnings.

The extent to which there are conflicts of interest in FDA hearings was explored in a lengthy article beginning with a front-page headline piece in *USA Today* on 25th September 2000.[lxviii] This maintains that it has become almost standard practice for advisers to the FDA to have a direct financial interest in the drug or topic they are asked to evaluate. The process of waiving conflicts of interest has become a mere formality. The FDA response to questions on this point is that the best experts for the FDA are often the best experts to consult with industry. But this is not always the case. It is not difficult to find others without the same ties to industry.

Since the controversies surrounding the Prozac and breast implant cases, the FDA “has stopped releasing details on conflicts because of concerns about violating the privacy rights of committee members.”[lxix] This concern is difficult to understand. Exactly what privacy rights are involved here? Similar controversies were being voiced in Britain at almost exactly the same time in connection with a new vaccine for meningitis C.[lxx]

Regulators and Friends

Following our healthy volunteer study, I wrote to the MCA, who now faced two studies showing Zoloft could trigger serious agitation.[lxxi] The MCA responded that a series of epidemiological studies indicated there was no problem. When pushed to name these epidemiological studies, they offered six names—essentially the studies Andy See had offered in Forsyth.[lxxii] One was the Jick study, which all but proved that Prozac caused suicide. Another was the Fava and Rosenbaum study, but most analyses of this accepted that it also indicated that Prozac did induce suicidality. The third and fourth were the Leon and Warshaw and Keller studies, but as we have seen in chapter 8, whatever these are, they are not epidemiological studies. The fifth, a British post-marketing surveillance study, compared SSRIs to each other using the reports of primary care physicians.[lxxiii] If extrapolated to the population at large, the rates cited would have trebled British national suicide rates. The final "study," by Ashleigh and Fesler, was a one-column letter in the *American Journal of Psychiatry* looking retrospectively at 206 patients who had been put on Prozac. Even Lilly had not used this in their defense.[lxxiv] The MCA failed to acknowledge two other genuinely epidemiological studies which had by this stage been published. One showed increased rates of suicidal acts on SSRIs[lxxv] and the other increased rates of suicide on SSRIs.[lxxvi]

This regulatory response is deeply problematic. It seems to me that there are only a few ways to interpret this specific MCA response. One would seem to be that they are incompetent. A second is that they are under pressure or rushed. A third option is that they have taken the word of some advisors that these are epidemiological studies that do not indicate a problem. In a world where advisors did not have conflicts of interest, this might have been reasonable. A fourth option is that they have taken the direct word of pharmaceutical companies that these are epidemiological studies.

When I first wrote to the MCA asking for any other studies on file with similar results to our healthy volunteer study, they responded that it would take some time to get back to me with an answer. They wrote to the SSRI companies and asked them for details of the results from their healthy volunteer studies. Four months later, I got my reply—a set of company assessments of what

their data revealed. None of these company assessments mentioned any difficulties or hazards; not even Pfizer's, where I knew there had been several disturbing healthy volunteer studies. Specifically challenged on the Hindmarch study, the MCA later revealed that they had acquired a copy of this study with a "pattern of severe adverse side effects and drop outs."[lxxvii] But had they only received it in response to my pressure? Everything about their response indicated that this was probably the case; regulators in Australia, for instance, did not appear to have a copy of this study.[lxxviii] It later transpired that the MCA possessed a four-page *summary* of the Hindmarch study. Company healthy volunteer studies from this period typically contained well over a hundred pages.

The e-mails within the FDA and between the FDA and Lilly on Prozac in the early 1990s had referred to a number of FDA personnel, including Paul David, Martin Brecher, and Paul Leber. Paul David had since become a vice-President of Lilly. Brecher had gone on to work with Janssen and later Astra-Zeneca. And in 1998, Paul Leber left the FDA and set up his own consulting firm. His first customer—and for a period his only one—was Pfizer.

The migration of FDA officials into industry will worry some. In Britain the trend was just the opposite. When writing to the MCA, I was writing to Keith Jones, who had formerly been in Merck. In early 2001 Ian Hudson, the former head of international safety for SmithKline, became head of the licensing division of the MCA. A few weeks beforehand, Hudson, still at SmithKline, had been deposed in the Tobin case, in which all of the themes of this chapter came to a head.

Tobin v. SmithKline

In February 1998, Donald Schell, a 60-year-old living in Gillette, Wyoming, became withdrawn and began to complain to his wife Rita of difficulty in sleeping. Schell first suffered from his nerves in the mid-1980s, with approximately five subsequent nervous episodes centred on work stressors or

bereavements. Don and Rita appeared to most of those who knew them to be a close couple. They were married for 37 years. They had two children, Michael and Deborah. Deborah married Tim Tobin in 1992 and in 1997 she gave birth to the Schell's first grandchild, Alyssa. Deborah and Alyssa, now nine months old, came down from Billings, Montana to stay for a few days with Don and Rita in February 1998.

Don's means of handling his nerves was to take time off work, as he could easily get someone to deputize for him. He went for walks with his wife and spent time talking with friends or with Tim, if he was around, in addition to taking care of his diet. He had got on well with a Dr. Suhany in 1990, so if he remained low after a week or two, either Rita or Don himself would suggest going along to see the doctor. Suhany had first put Schell on Prozac and noted that it made him tense, anxious and jittery, despite the fact that he was on several antidotes such as Inderal, Ativan, and Desyrel. Suhany stopped Prozac and put Schell on imipramine, to which he responded rapidly.[lxxix] What Suhany didn't know was that Schell might have even been hallucinating while on Prozac. Having responded to imipramine in 1990, in two further brief episodes in the 1990s Schell was put on tricyclic antidepressants and again responded rapidly.

In February of 1998, when Schell began to complain about his sleep, he and Rita went to see a primary care physician, Dr. Patel. Dr. Patel did a thorough examination, which included rating scales that indicated Schell's main difficulty was poor sleep and that he felt hopeful about the future and thought well of himself. Patel diagnosed an anxiety state and, unaware of the significance of a prior adverse response to Prozac, put Schell on Paxil, without any covering antidotes. Forty-eight hours later Don Schell put three bullets from two different guns through Rita's head, and then through Deborah and Alyssa's heads before shooting himself.

After more than a year in a mental wilderness, Tim Tobin sought out Andy Vickery and took an action for wrongful death against SmithKline Beecham,

then in the process of becoming Glaxo-SmithKline, the worlds largest pharmaceutical company. I was retained in the case.

The Toronto Affair[lxxx]

At the end of November 2000, the University of Toronto Department of Psychiatry invited me to speak at a 75th anniversary meeting on the theme "Looking Back: Looking Ahead." Charles Nemeroff was also on the program.

A year before, I had been appointed to the University of Toronto as a Professor of Psychiatry in the Mood and Anxiety Disorders Programme at the Centre for Addiction and Mental Health (CAMH).[lxxxi] I was waiting for my visa. A week after the Toronto meeting, I was due to give an annual guest lecture plus seminars on the history of psychiatry at Cornell University Medical School, New York. I arranged to give the same talk in both places, visiting Pfizer's New York Zoloft archive in between.

The day before the Toronto meeting, I interviewed a psychologist for a position on the program I would be running, considered décor for my new office, and discussed the practicalities of moving from Britain to Canada with David Goldbloom, the physician in chief at CAMH, whose budget would cover part of my salary. I discussed the SSRI medico-legal cases I was involved in and he seemed to have no concerns. Some members of the university department on the day of the meeting were in Indianapolis discussing "work product" with Lilly, which had funded research in the department. In the previous year, the mood disorders program had received over 50% of its research funding from pharmaceutical companies.

The talk I gave to Toronto and Cornell had first been worked up for a meeting for Astra-Zeneca. My lecture outlined my forthcoming Harvard University Press book *The Creation of Psychopharmacology.*[lxxxii] I reviewed developments over 50 years of psychopharmacology, the key drugs, the development of clinical trials, and the subsequent development of conflicts of

interest. I touched peripherally on the central claims of this book—that SSRIs can make people suicidal, and that since the problem arose there had been no research to map its dimensions and decide how best to minimize the risks posed by these drugs.[lxxxiii] The post-meeting feedback forms I received from Toronto some weeks later showed that my talk had rated the highest for content—and Nemeroff's the lowest.

After my lecture in New York, Jack Barchas, head of the psychiatric department in Cornell and editor of the *Archives of General Psychiatry*, told me that my work would be remembered 100 years from now, unlike little else now happening in the field.

Bob Michels, the dean of Cornell, attended a meal after my talk there. He immediately asked me what had happened in Toronto. Surprised, I said I had delivered the same talk he had just heard. I outlined to Michels and others my encounter earlier in the year with Nemeroff, and how after the lecture in Toronto Goldbloom told me he took exception to my claim that SSRIs could make someone suicidal with the implication—as he put it—that Lilly had known about it. The day of the talk in Toronto, according to Nemeroff's lawyer Nina Gussack, Nemeroff had talked to some people in the University about "Healy" and was under the impression that decisions had been taken.[lxxxiv] In a subsequent letter, Goldbloom indicated Nemeroff had been only one of the people who talked to him. He believed that these people had independently spoken to him. Had they—or had they all, in one form or another, encountered Nemeroff?

Michels made it clear that I had been fired. I flew home from New York the following day to find an email from Goldbloom: "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. While you are held in high regard as a scholar of the history of modern psychiatry, 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."

What could explain what had happened? The University of Toronto was still embroiled in the affair of Nancy Olivieri, a researcher dismissed for publishing data on adverse events from a clinical trial.[lxxxv] An international outcry foreced her reinstatement, and a new Dean pledged to uphold the core values of a university.[lxxxvi] Another Olivieri case would be a disaster for the University. It might be an even bigger disaster for Lilly, Pfizer, and SmithKline, because it was just the kind of story a jury could understand only too well.

The day after my talk in Toronto, just as I entered Pfizer's archive to seek out their healthy volunteer studies, Nemeroff had spoken at length on "Healy and his views" before a group of psychiatrists in New York at a council meeting of the American Foundation for Suicide Prevention. Sometime between Friday and Tuesday, when I lectured in Cornell, a senior figure in US psychopharmacology called senior figures in Cornell telling them, my informant suggested, that "Healy was manic-depressive, violent and a peddler of junk science," intimating that my lecture should be cancelled.

I learned most of this within days of receiving the Goldbloom e-mail message. When overtures to senior CAMH and University figures brought no constructive response, I wrote to CAMH and the University, suggesting that the picture might be a more complex one than they initially appreciated. Given that Lilly withdrew their funding from the Hastings Centre after an article I had written covering the same ground, the likely press interpretation would be that the institution had been worried about the threat to funding of its psychiatric department.[lxxxvii] Had Goldbloom unwittingly maneuvered the University of Toronto into the extraordinary position of compromising a witness in a legal case?

What happened to Peter Breggin in the Fentress case was a cautionary tale. But there was more. Before he bowed out of the Prozac debate in the mid-90s, Martin Teicher had appeared in one case, the Greer case. It is clear from his deposition in this case that in 1996 he still held to his original position on

Prozac's capacity to trigger suicidality.[lxxxviii] At his deposition, Nina Gussack, the attorney for Lilly, went through his six cases in detail.

Teicher, as it turned out, had sent his second case to Rosenbaum for another opinion. Rosenbaum claimed the patient said, "I never thought I was any more suicidal on Prozac than I was before or after, but I suppose Dr. Teicher is more sensitive to this issue." Alarmed at the implications, Teicher had seen the patient again after receiving a letter from Rosenbaum. Faced with his medical records, the man apparently did remember just how bad it had been on Prozac. Teicher's notes included details of phone calls from the man's mother, confirming that he had been significantly worse while on Prozac than ever before.

In a letter to Teicher, Rosenbaum "recognized" that a patient is not always an accurate historian. As far as he could gather, the patient had gone on Prozac again without becoming suicidal. Teicher's medical notes revealed a different picture. Faced with a man who did not connect his suicidality to his Prozac intake, Teicher had in fact tested him out on Prozac again a year later, and he had again become suicidal. So either the case was strengthening with this rechallenge or Teicher had been fooled. I recognized this failure to remember as one of the difficulties my patient Tony L. had after becoming suicidal on Prozac. It was as though Prozac, like childbirth, produced state-dependent changes; afterwards the individual sometimes just didn't remember what it was like. But how did Gussack come to have this supposedly confidential clinical correspondence?

On the second day of the deposition, Teicher and Gussack worked their way from case 2 through to case 6. Teicher stated that he had been instructed by his attorney to discuss only those details of this 6th case which had appeared in print. Gussack nevertheless asked about the malpractice suit which, she asserted, the patient had filed. She inquired about an ongoing legal matter regarding his registration with the Board of Registration in Medicine in Massachusetts.

Gussack asked: “Would you agree, doctor, that she complained you were negligent in your prescribing of multiple medications for her at the same time?” “Did she also allege in her deposition that you had engaged in multiple acts of sexual relations with her?” “Is it accurate to state that ..you described this [patient] as a grand hysteric… who would make up all sorts of things for attention…. that [she] had serious problems with reality testing, distinguishing fantasy from reality in all areas?” “You said that Jane Doe would call you at home… throughout the course of the time you were treating her?” “”She had a great deal of difficulty at night… she was ‘very lonely, very frightened, often very suicidal after her husband had gone to sleep.’”

“Doctor, it is true, isn’t it, that in the course of the malpractice suit.. patient number 6 alleges that you had sexual relations with her starting in the fall of 1984…. That you had sexual relations with her at the Battle Green Hotel… Have you denied in your testimony... that you had any inappropriate touching or kissing with patient number 6… that on three or four occasions she had sexual relations with you at your home…., that you engaged in oral sex, intercourse and anal intercourse with you on a number of occasions… that you had sexual relations with her in your office countless times… that you have given her gifts... an artificial plant.. a foldout fan... a pair of earrings... birthday cards, signed ‘Love Marty’... cassette tapes of recordings of you playing the guitar?”

This was late on the second day of questioning. Even the court stenographer was getting worked up and misplacing pronouns. Teicher refused to answer anything against a backdrop of Andy Greenwald, counsel for Greer, saying: “I don’t know why I keep saying objection. I have a continuing objection.”

Most clinicians reviewing the bare details of this kind of case, unaware of the context, would assume a considerable possibility that few of the things being aimed at Teicher were in fact true. This woman had been described as a borderline patient in the 1990 paper, and “boundary problems,” as they are called, are a feature of managing just this kind of patient. The difficulty for Teicher was that even if nothing was true, given the Breggin example, he

couldn't win on a witness stand, even though the Massachusetts Board of Registration had decided that there was no malpractice.[lxxxix]

A few weeks before this deposition, he received further news. Divorced, Teicher lived close to his former wife and helped out with the children. But then his wife moved—to a post in oncology in Indianapolis with Lilly.

There was a good chance the first question I would face on cross-examination in the Tobin case would be: "Dr. Healy, isn't it true that you were recently sacked from the University of Toronto?" Journalists were already asking questions of the University of Toronto, CAMH, and Nina Gussack. Faced with an almost complete lack of response from the University of Toronto or CAMH, I had little option but to raise the affair pre-emptively in my deposition in the Tobin case at the end of March, and then to answer media questions on the issue. A few weeks later, in response to an application from SmithKline, Judge William Beaman issued a gag order that prohibited the lawyers from talking to the media and from raising the issue of my employment status in any legal proceedings.

Showdown in Cheyenne

The Tobin case was heard in Cheyenne Wyoming from May 21st, 2001 to June 6th. Just before the case started, a Supreme Court judge in New South Wales, Australia, delivered a verdict making it clear that in his opinion David Hawkins, a 73-year-old man who had murdered his wife the day after going on Zoloft, having had a prior history of an adverse response to Zoloft, would not have done so had he not been put on Zoloft. But it was too late to factor this into the Tobin case.

The jury of five women and three men heard first from Vickery and Fitzgerald for the plaintiffs. The surviving members of the Tobin and Schell families testified. There was expert input from Don Marks, who had previously worked as a safety officer for Roche Pharmaceuticals, Terry Maltsberger from

Harvard, and me. They heard the physician Dr. Patel say that if he had been warned, he would have taken even more care than he had originally taken.

SmithKline put forward a series of experts: John Mann from Columbia, Alan Fraser from San Antonio, Philip Wang from Harvard and Kenneth Tardiff from Cornell, as well as David Wheadon, Ian Hudson and others from the company.

The defense rested on a number of claims. One was that Don Schell was chronically depressed and ideally should have been maintained on antidepressants for the rest of his life from the time he had become depressed first. Part of the basis for this claim lay in a study by Montgomery in which patients who had responded to Paxil were after several months re-randomized to either Paxil or placebo. Those who went onto placebo got unwell, leading Montgomery and SmithKline to claim that Paxil not only treated, but prevented further episodes of depression[xc]. On the basis of this study, the FDA and MCA had licensed SmithKline to make these claims. But in the light of 85% rates of physical dependence reported in SmithKline's studies with healthy volunteers, this claim was extraordinary.

A second claim was that Montgomery and Lopez-Ibor had independently analyzed the SmithKline clinical trial databases and their analyses had demonstrated that Paxil did not induce suicide. In fact as will become clear, unbeknownst to the plaintiffs, there was an extraordinary set of problems with these figures that only became obvious after the trial (chapter 11).

A third claim was that a report—the Cheng report, which contained the reports to SmithKline of suicides or homicides on Paxil—found similar rates as happened in the population at large.[xci] But this defense failed to take into account that the rates at which these events were likely to be reported to SmithKline were at best one in ten of those happening and perhaps even as bad as one in one hundred of those happening. Apparent rates equivalent to the population at large might even be consistent with an epidemic of violent deaths.

In the face of SmithKline documents showing that investigators and company personnel had coded clinical trial reactions, including akathisia and hallucinations, as definitely caused by Paxil, the company argued that it is not possible to establish causality in an individual case—this can only be done by randomized controlled trials.

This strategy came through at its most chilling, perhaps the most chilling moment in the entire trial, in exchanges between Ian Hudson and Vickery. Having repeatedly told Vickery that SmithKline could never decide in a case of suicide whether their drug was to blame, Hudson was faced with the following:

Q. Okay. So, your view is: It's simply impossible for SmithKline Beecham to decide whether Paxil did or did not contribute to the homicidal or suicidal behavior of any one given individual; is that your testimony?

A. We would certainly gather all the information, but on an individual case basis it would be impossible to decide whether paroxetine caused an event or not.

Q. Okay. Now—hold on just a minute… If you were to get Exhibit Two there, the Aggression Study [Cheng Report]—I've lost my page. Bear with me just a second. Okay. Would you turn to page twenty-one of sixty-three? Are you there with me?

A. Yes.

Q. Now, is it impossible for SmithKline Beecham to determine whether the patient identified in the fifth report on the bottom of that page, whether his behavior was caused or was not caused by Paxil?

A. On an individual case basis, it would be impossible to say whether a drug caused an event.

Q. Okay. Do you know if that patient, that's reflected down there, is the decedent of my client? Is that Donald Schell?

A. I believe it is, yes.

Q. You're telling me, under oath, it's simply impossible for SmithKline Beecham to decide whether Paxil did or did not cause Mr. Schell to murder his wife, his daughter, his granddaughter and then to commit suicide; is that right, sir?

A. It is impossible, on an individual case basis, from individual reports, to assign causality especially in a very complicated area such as this. That's why, when we have issues, we review all the available data and make a determination, on the basis of all the available data, whether there is an issue or not.

Q. Okay. Do you believe that it is possible that Paxil has caused any person, worldwide, to commit an act of homicide or suicide?

A: I have seen no evidence to suggest that at all.[xcii]

Hudson was opening up an extraordinary black hole here. No matter how many physicians or others reported to SmithKline suicides or homicides they thought related to the drug, SmithKline would deny any evidence for causation while there was no randomized controlled trial evidence. The fact that they had never undertaken any trials and had no plans to do so smacked of washing their hands in the face of a crucifixion. In many internal assessments at the time, companies had in fact overridden the opinions of their investigators that the drug had not caused the problem and coded the reactions as caused by the drug—but according to this new defense, even these assessments were not valid.

The jury disagreed with Hudson. On June 6th, having recessed for less than three hours after a two-and-a-half-week trial, they returned a guilty verdict against SmithKline and an award for damages four times greater than the biggest previous award in Wyoming—a first-ever verdict against a pharmaceutical company for a psychiatric side effect of a psychotropic drug.

Is Freedom in Toronto Academic?

The Tobin verdict seemed to have no impact in Toronto. There were no overtures from the University or CAMH to look at the issues afresh. Quite the contrary: one of the few outsiders to support the CAMH and University position now appeared on the scene. A Dr. James Coyne wrote to the *University of Toronto Bulletin* and to the *Globe and Mail,* essentially to say

that the only surprising thing about the Healy affair was that the University had sought to hire me in the first instance. That the research design of my healthy volunteer study was flawed. That I had not declared conflicts of interest. Coyne claimed the *Globe and Mail* approached him when the affair first surfaced but then accused him of maintaining his views only because he was in receipt of pharmaceutical company funds. This he denied. It later transpired that Coyne was a member of advisory boards for both Lilly and Solvay-Duphar. He also had links to Chamberlain Communications. Apparently senior figures in CAMH or the University of Toronto suggested to the *Globe and Mail* that Coyne be approached to get another side on the Healy affair.

The position taken by the University and CAMH at this point was that the clinical domain produced its own set of particular issues when it came to academic freedom. The usual rules, it was suggested, couldn't apply when vulnerable patients were likely to be affected by what was said. To allow a critic like me to denigrate a treatment like the SSRIs would be like letting a fool cry "Fire!" in a crowded theatre.

The need for extra caution in the clinical domain has long been recognized. This is precisely why regulations have been put in place—to limit the abilities of quacks to sell worthless treatments to vulnerable people. But speaking out about the hazards of treatment was exactly why drug treatments were made prescription-only. Keeping quiet about a known hazard *de facto* breaks the spirit of the law, whatever the letter of the law may be.

By this time, the Canadian Association for University Teachers (CAUT) had lobbied the University and others on my behalf. They got no more response than I. In September a letter signed by 29 senior figures in the field—including two Nobel Prize winners, former presidents of the American Psychiatric Association, the American College of Neuropsychopharmacology, and a range of other psychiatric and psychopharmacological organizations worldwide—was sent to U of T President Robert Birgenau, protesting the violation of academic freedom involved in "the Healy case." There was input from Europe, North and South America, Japan, China, and Australia.

Birgenau's response suggested these signatories were not fully aware of the issues in the case. Two weeks later, supported by CAUT, I filed a legal action against the university, involving a first-ever claim for violation of academic freedom, with further claims for breach of contract and libel.[xciii] This seemed the only way to find out more about the issues in the case.

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i Deposition of D Healy in *Miller V Pfizer*, Boston, March 29th 2000, page 341. Unfortunately further details of this study remain unavailable due to a confidentiality order.
ii Deposition of D Healy in *Miller V Pfizer*, Boston, March 29th 2000.
iii In the case of the FDA, the details were faxed directly to David Graham and Tom Laughren.
iv The full correspondence is available on *socialaudit.org.uk* and on
v Healy D, Trial testimony in *Tobin v SmithKline Beecham*, Cheyenne, May 2001.
vi Healy D, Nutt D. British Association for Psychopharmacology Consensus on Childhood and Learning Disabilities Psychopharmacology. *J Psychopharmacology* 11, 291–4 (1997).
vii Fisher R, Fisher S. Antidepressants for children. Is scientific support necessary? *Journal of Nervous and Mental Disease* 184, 99–102 (1996). Accompanying commentaries from Leon Eisenberg and Edmund Pellegrino on pages 103–5 and 106–8 make this set of contributions a benchmark for what was happening in the area of pre-adult antidepressant prescribing in the 1990s. See also Ambrosini PJ. A review of pharmacotherapy of major depression in children and adolescents. *Psychiatric Services* 51, 627–33 (2000).
viii Emslie GJ, Rush AJ, Weinberg WA *et al.* A double-blind, randomized, placebo-controlled trial of fluoxetine in children and adolescents with depression. *Archives of General Psychiatry* 54, 1031–37 (1997).
ix Shute N, Locy T, Pasternak D. The perils of pills. The psychiatric medication of children is dangerously haphazard. *US News and World Reports* March 6th 44–50 (2000).
x Deposition of Douglas Geenens in *Miller Vs Pfizer* (1999).
xi Deposition of Matthew Miller's grandmother in *Miller Vs Pfizer*.
xii Deposition of Hilary Burton in *Miller Vs Pfizer*, February 15th 2000.
xiii May 27th 1999.
xiv Expert opinion of Parke Dietz in *Miller Vs Pfizer*. Dietz had some years before offered the view that Anita Hill might be suffering from an erotomanic fantasy for Clarence Thomas and that her delusional beliefs led to the claims against him—see Kutchins S, Klerk S. *Making us Crazy* (1998).
xv Pfizer clinical trial database December 1991.
xvi Exhibit 40 in *Miller Vs Pfizer* at page 23. The publications stemming from these trials, however, only refer to one suicidal act, other than obliquely; one article on the side effects of sertraline refer to the fact that no-other side effects occurred in more than 10% of subjects.
xvii Exhibit 40 in *Miller Vs Pfizer* at page 17, 18 & 20.
xviii A subsequent trial Keller MB, Ryan ND, Strober M *et al.* Efficacy of paroxetine in the treatment of adolescent major depression: a randomised controlled trial. *Journal of the American Academy of Child and Adolescent Psychiatry* 40, 762–72, (2001) on paroxetine in children also reported rates of suicidal acts much higher on paroxetine than on placebo. The authors dismissed this finding by saying that in their opinion these acts were not caused by the drug.
xix Fisher S, Kent TA, Bryant SG. Postmarketing surveillance by patient self-monitoring: Preliminary data for Zoloft versus fluoxetine. *Journal of Clinical Psychiatry* 56, 288–96 (1995). See also Fisher S, Bryant SG, Kent TA. Postmarketing surveillance by patient self-monitoring: trazodone versus fluoxetine. *Journal of Clinical Psychopharmacology* 13, 235–42 (1993). See also Valenstein E. *Blaming the Brain*. The Free Press, New York (1998).
xx Communication from Allison Sesnon, the program maker.
xxi Poitras C, February 25th 2000. Prozac Defence brings Acquittal. *The Hartford Courant*.
xxii The details in this case remain confidential but I was involved as an expert witness.
xxiii Swiatek J. Lilly's legal tactics disarmed legions of Prozac lawyers. *Indianapolis Star*, Sunday April 23rd A 1 & 18–19 & Monday 24th A1 and A8 (2000).

xxiv Glenmullen J. *Prozac Backlash*. Simon & Schuster, New York (2000).
xxv Teicher MH, Klein DA, Andersen SL, Wallace P. Development of an animal model of fluoxetine akathisia. *Prog Neuropsychopharmacol Biol Psychiatry* 19, 1305–19 (1995).
xxvi Young JM, Barberich TJ, Teicher MH. US Patent number 5, 708,035. January 13th (1998).
xxvii Martin Teicher subsequently went on to work on an isomer of Ritalin for Sepracor.
xxviii John Cornwell had originally planned to call *The Power to Harm* "The Prozac Trials." His publisher objected. Cornwell felt that a number of reviews of his book had been strategically placed. He later wrote *Hitler's Pope*, a book that implicated the Catholic Church in the Holocaust, if only by failure of omission, and blocked efforts to beatify Pius XII. This did not make him popular in the Vatican, but overall in his estimation the Vatican was much less of a problem to deal with than a pharmaceutical company can be.
xxix I am indebted to KM for copies of this material from *Newsday*.
xxx Letter from Robert Schwadron to Jamie Talan *Newsday*, April 6th 2000.
xxxi Garnett LR. *Prozac Revisited*. As drug is remade, concerns about suicides surface. May 7th, page 1 et seq. (2000).
xxxii Young JM, Barberich TJ, Teicher MH. US Patent number 5, 708,035. January 13th at page 10 (1998).
xxxiii *Ibid.*, page 12.
xxxiv Tollefson G. Letter: Article on Prozac ignored overwhelming evidence. *The Boston Sunday Globe*, May 21st (2000).
xxxv This building is striking partly because it is derelict, and at night shows as a darkened and jagged stump on the skyline.
xxxvi This use of the word pharmacologist was how Dr McNeil's lawyer, Lawrence Finn, designated him; see deposition of D Healy in *Berman Vs Eli Lilly and Company et al,* September 25th 2000.
xxxvii Deposition of Darryl Pure in *Berman Vs McNeil, Pure & Eli Lilly*. April 18th & June 11th 1998.
xxxviii Deposition David McNeil in *Berman Vs McNeil, Pure & Eli Lilly*. April 22nd 1998.
xxxix Murgatroyd GW, Barth KA, Vickery A, Chang RK. Independent action to set aside judgement for fraud on court. District of Hawaii (2000).
xl The cardiac profile of psychotropic drugs has been a problem since 1996 when sertindole, an antipsychotic made by Lundbeck and which Abbott hoped to market in the US, was shown to produce the cardiac abnormality later found in R- fluoxetine. No one knew whether this was a real problem or not, but it was enough to stall sertindole's licensing. The company who benefited from this was Lilly, whose antipsychotic olanzapine in consequence enjoyed a free run. The extraordinary story behind this anomaly illustrates perfectly where the power of regulation at present lies—before a drug is licensed. The details are in chapter 6 of Healy D. *The Rise of the Antipsychotics*. Harvard University Press (2001). As Prozac, which almost necessarily has the same cardiac profile that would later delay development of R-fluoxetine, doesn't cause cardiac problems, the question arises whether Lilly were using this anomaly to get rid of R- fluoxetine or whether they were truly jinxed.
xli Pierson R. Sepracor falls as Lilly pulls plug on version of Prozac. October 19th Reuters (2000).
xlii Information from Lilly website—October 2000.
xliii Exhibit 10 in Deposition of J Potvin in *Fentress Vs Eli Lilly*.
xliv Fludzinski L, Deposition in *Fentress Vs Eli Lilly*, Exhibit 28.
xlv Montgomery DB, Roberts A, Green M, Bullock T, Baldwin D, Montgomery SA. Lack of efficacy of fluoxetine in recurrent brief depression and suicidal attempts. *European Archives of Psychiatry and Clinical Neuroscience* 244, 211–15 (1994).
xlvi Exhibit 4 in the Deposition of L Thompson in *Fentress Vs Eli Lilly* (1994).
xlvii Exhibit 21 in the deposition of Joachim Wernicke in *Fentress Vs Eli Lilly*. The significance level in favor of placebo is cited as p= 0.006.
xlviii Baldwin D. The treatment of recurrent brief depression. European College of Neuropsychopharmacology Meeting London, Sept 24th (1999).
xlix Healy D. Testimony in *Tobin vs SmithKline*, Cheyenne, May 23rd 2001.
l Details from David Baldwin, an investigator on the study.

li Verkes RJ, Van Der Mast RC, Hengeveld MW, Tuyl JP, Zwinderman AH, Van Kempen GM (1998). Reduction by paroxetine of suicidal behavior in patients with repeated suicide attempts but not major depression. *American J Psychiatry* 155, 543–7.
lii Exhibit 16 in Deposition of A Webber in *Fentress Vs Eli Lilly*.
liii Montgomery SA, Dunner DL, Dunbar G. "Reduction of suicidal thoughts with paroxetine in comparison to reference antidepressants and placebo". *European Neuropsychopharmacology* 5, (1995), 5-13.
liv Lopez-Ibor JJ. Reduced suidality on paroxetine. *European Psychiatry*. 1993; 1 (Suppl 8): 17s-19s.
lv Dunner D and Kumar R. Paroxetine: A review of clinical experience (1998) *Pharmacopsychiatry 31, (1998),* 89-101
lvi Letter from Andrea Smith Lilly to Sara [sic] Boseley 5/19/00.
lvii Deposition of Daniel Casey in *Miller Vs Pfizer*, April 2000, 69.
lviii Mann J (2000). Deposition of J Mann in *Miller Vs Pfizer*, 65.
lix Lane R (1999). Deposition of R Lane in *Miller Vs Pfizer*, 96. Wheadon D (2000). Deposition of D Wheadon in *Tobin vs SmithKline*, 44. Beasley C (2000). Deposition of C Beasley in *Espinoza vs Eli Lilly*, 10.
lx I have these details from George Beaumont and several others.
lxi This conversation was witnessed by Claus Langmaack. It was recorded in note form immediately afterwards by me. Obviously such conversations are open to misinterpretation and it cannot be excluded that Dr Nemeroff was simply concerned about my welfare.
lxii "Speaking on behalf of Lilly, Charles Nemeroff . . was quick to discredit the anecdotal testimony of alleged Prozac victims. Asserting that anecdotal reports fail to establish cause and effect, Nemeroff said that double-blind, placebo controlled trials were necessary to prove such a link. Criticizing studies of Prozac's adverse effects that were based on anecdotal evidence with small numbers of patients, Nemeroff said that Teicher's study has launched 'a maelstrom of activity' in the lay press. Teicher's conclusions were based on six patients who had 'multiple complicating factors,' including alcohol abuse, multiple personalities and 'other factors known to be associated with suicidality,' Nemeroff maintained. He also emphasized that 'suicidality is part and parcel of this disease [depression]' and therefore it is difficult to attribute suicidal behavior to the drug." *Health News Daily* September 23, 1991.
lxiii C Nemeroff as of the summer of 2001 listed himself on conflict of interest statements as a major equity shareholder in Lilly, Bristol-Myers Squibb, Forest, Organon, SmithKline Beecham, Astra-Zeneca, Pfizer, Janssen, Wyeth-Ayerst & Merck. In addition he has grant/research support and other financial and material support from the same companies. He is also a paid consultant for, on the speakers bureau for and receives direct payments for talks from the same companies. Nemeroff said that under current conflict of interest guidelines being a major equity shareholder means owning $10,000 worth of stock or more. That he had got a few shares from Eli Lilly some years before and when he found that they had increased in value to over $10,000 he declared this. (Again my recollection of the details of what he said being a major equity shareholder meant is open to error, but the listing of CN's links to companies was prepared by him and not me).
lxiv *T.E.N.* September issue, volume 2, number 9 (2000).
lxv Tollefson GD, Rosenbaum JF. Selective serotonin reuptake inhibitors. In Schatzberg AF, Nem eroff CB (eds.). *The American Psychiatric Press Textbook of Psychopharmacology*, APA Press Inc, Washington D.C., 219–37 (1998).
lxvi Declaration in support of plaintiff's opposition to defendant's motion for partial summary judgment on plaintiff's inadequate-warning claims, in *Motus Vs Pfizer* (10/30/2000).
66. According to Martin Teicher, there was for example a phone call to Joe Coyle and other efforts to get MT to drop these matters for the sake of his career and the public good.
lxvii According to Martin Teicher, there was for example a phone call to Joe Coyle and other efforts to get MT to drop these matters for the sake of his career and the public good.
lxviii Cauchon D. FDA advisers tied to industry. *USA Today* September 25th page 1; & Cauchon D Number of drug experts available is limited. Page 10 (2000).
lxix In Cauchon D Number of drug experts available is limited. Page 10.
lxx Calvert J, Johnston L (2000). *Sunday Express*, August 6th pages 1, 2, 8, 9 & 32. Bright M, McVeigh T (2000). Meningitis advisers funded by drug firms. *Observer* September 3rd, pp.10; Boseley S. Column in *Guardian* Newspaper, G2 Section, September 5th (2000).
lxxi The entire correspondence is available on *socialaudit.org.uk* and.

lxxii Letter from Dr K Jones, Medicines Control Agency, August 23rd 2000.
lxxiii Price *et al.* PMS Mackay FJ, Dunn NR, Martin MR, Pearce GL, Freemantle SN, Mann RD. Newer antidepressants: a comparison of tolerability in general practice. *British Journal of General Practice* 49, 892–96 (1999).
lxxiv Ashleigh EA, Fesler FA. Fluoxetine and suicidal preoccupation. *American Journal of Psychiatry* 149, 1750 (1992).
lxxv Donovan S, Clayton A, Beeharry M, Jones S, Kirk C, Waters K, Gardner D, Faulding J, Madely R (2000). Deliberate self-harm and antidepressant drugs. Investigation of a possible link. *British Journal of Psychiatry* 177, 551–56.
lxxvi Donovan S, Kelleher MJ, Lambourn J, Foster R (!999). The occurrence of suicide following the prescription of antidepressant drugs. *Arch Suic Res* 5, 181–92.
lxxvii Letter from Dr K Jones, Medicines Control Agency, August 23rd 2000.
lxxviii Correspondence from Tania Evers of New South Wales Legal Aid.
lxxix Deposition of Dr Suhany in *Tobin vs SmithKline* 2000.
lxxx Most of this book antedates the events of November 30th.
lxxxi Formerly the Clarke Institute.
lxxxii Healy D. *The Creation of Psychopharmacology*. Harvard University Press, Cambridge Mass, 2002.
lxxxiii It was not a talk about SSRIs and suicide
lxxxiv Healy D (2002). Conflicting interests in Toronto: The Anatomy of a Controversy at the Interface of Academia & Industry. *Perspectives in Biology & Medicine*.
lxxxv Barer ML, McGrail KM, Cardiff K, Wood L, Green CJ (eds) (2000). *Tales from the Other Drug Wars*. The Centre for Health Services and Policy Research, Vancouver.
lxxxvi Thompson J, Baird P, Downie J (2001). *The Olivieri Report*. James Lorimer & Co., Toronto; Turk JL (ed) (2000). *The Corporate Campus. Commercialization and the Dangers to Canada's Colleges and Universities*. James Lorimer & Co, Toronto
lxxxvii McIlroy A (2001).. *Globe and Mail*.
lxxxviii Deposition of Martin Teicher in *Greer Vs Eli Lilly*, October 29th and 30th 1996.
lxxxix One of the witnesses in favor of Teicher had been Jerrold Rosenbaum.
xc Montgomery SA, Dunbar GC. Paroxetine is better than placebo in relapse prevention and the prophylaxis of recurrent depression. *International Clinical Psychopharmacology* 1993, 8, 189–95.9
xci Comment on the Cheng Report in the Expert Report of K Tardiff in *Tobin vs SmithKlline Beecham*, April 3rd 2001.
xcii Deposition of Ian Hudson in *Tobin vs SmithKline* Beecham, December 15th 2000, 30–33.
xciii Healy D. Conflicting interests in Toronto: the anatomy of a controversy at the interface of academia and industry. *Perspectives in Biology and Medicine* 2002.