Brain-Disabling Treatments in Psychiatry

14 - Drug Company Deceptions

Drugs, Electroshock, and the Psychopharmaceutical Complex


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Contents

14 Drug Company Deceptions 553

14.1 Relying on Junk Science 556

14.2 Eli Lilly and Prozac 558

14.2.1 Eli Lilly Knew From the Start that Prozac Acts Like A Stimulant 558

14.2.2 Eli Lilly Successfully Bamboozles the Legal System 560

14.2.3 Eli Lilly Acknowledges to the Food and Drug Administration (FDA) That Prozac Frequently Causes Depression 562

14.2.4 Eli Lilly Hides the Implications of Prozac-Induced Mania 563

14.2.5 Eli Lilly Confirms and Hides Prozac Overstimulation 564

14.2.6 Hiding the Risk of Prozac-Induced Mania and Aggression in Children 565

14.2.7 Eli Lilly and the FDA Ignore Reports of Aggressive Behavior on Prozac 565

14.2.8 Eli Lilly and the FDA Ignore Reports of Suicidal Behavior on Prozac 566

14.2.9 Eli Lilly Hides Increased Suicidality on Prozac in Controlled Clinical Trials 567

14.2.10 Eli Lilly Employees Express Shame 569

14.2.11 Adverse Reactions to Prozac in Eli Lilly’s Earliest Research 571

14.2.12 Prozac-Induced Aggression in Eli Lilly’s Earliest Animal Studies 572

14.2.13 British and German Regulatory Authorities Inquire About Prozac-Induced Stimulation, Agitation, and Depression 573

14.3 Eli Lilly Hides Akathisia 575

14.4 Lilly Covers Up Prozac Reactions 577

14.5 Similar Drug Approval Problems with Zoloft and Paxil 578

14.6 Prozac Interactions with Other Drugs 578

14.7 Prozac in Combination with Tricyclic Antidepressants 579

14.8 Eli Lilly Life-Threatening 580

14.9 Lilly Hides Deadly Drugs 583

14.10 Glaxosmithkline (GSK) and Paxil 585

14.10.1 Paxil Overstimulation 585

14.10.2 The Lacuzaong Case 586

14.11 Paxil and GSK Criticized By Medical Journals and Foreign Drug Regulatory Agencies 589

14.12 The Attorney Action Against Paxil 591

14.13 Britain Takes Action 593
14.1 Relying on Junk Science

Worse yet, as already emphasized in chapter 13, the FDA relies on the drug companies for the so-called science that is used to determine the safety and efficacy of drugs. On December 13, 2006, the FDA’s Psychopharmacological Drugs Advisory Committee held a public meeting to discuss and evaluate the risk of antidepressants causing suicidal behavior in adults. The FDA had already added a warning to antidepressant labels concerning drug-induced suicidality in children and youth under age 18. As I had at earlier FDA hearings on antidepressants, I made a brief, 3-min presentation. As I also had done on previous occasions, I emphasized that the FDA was relying too much on data generated, culled, and manipulated by the drug companies and that the agency ought to avail itself of experts like me, who had actually evaluated the junk science produced by the drug companies. I told the agency,

“Fifteen years ago, I warned the FDA and I warned the country in Toxic Psychiatry [19] that antidepressants were causing a stimulant, amphetamine-like syndrome that was resulting in suicide, violence, and murder. In 1994, in Talking Back to Prozac, I warned the country and the FDA, this time now with tens of scientific data, on the same issues.”

“During that period of time, I was asked to be - and this is very relevant to your deliberations - the scientific investigator for the combined Prozac suits, almost 200 of them. I got to look at all the sealed data that Eli Lilly didn’t want anybody else to see.”

“About 20 books later now, and a few dozen scientific studies and innumerable product liability suits where I’ve looked at sealed data, I have come to tell you that you are evaluating junk. You are evaluating carefully edited expurgated data that I have seen and you have not.”

“This is a most remarkable circumstance: that you... have

Chapter 14

Drug Company Deceptions

“Public Perception of US Pharmaceutical Industry at All-Time Low” (2005) [69] warned a headline in the Pharmaceutical Business Review. The business review explained,

“Increased safety warnings attached to some drugs (such as Roche’s Accutane and GlaxoSmithKline’s Paxil) and the complete market withdrawal of others (for example, Merck & Co’s Vioxx) have undermined consumer confidence in both the pharmaceutical industry and the products it produces. As a result, consumers now question whether pharmaceutical companies have their best interests in mind when marketing a product.”

On the brighter side, Pharmaceutical Business Review looks forward to the restoration of the public confidence. The drug companies have the leverage to accomplish this. Every area of modern psychiatry is permeated, and even inundated, with the influence of drug company money. As I began documenting in detail in 1991 in Toxic Psychiatry [19], worldwide clinical research, medical school research facilities and professorships, journal publications, conferences, and professional associations all, nowadays, depend on infusions of cash generated by the
sale of drugs. The Food and Drug Administration (FDA) itself now solicits funding from drug companies to expedite the process of drug approval.

As a recent study found (Cosgrove et al., 2006 [30]), even the development of official psychiatric diagnoses takes place under the sway of the pharmaceutical industry. The Diagnostic and Statistical Manual of Mental Disorders (DSM; American Psychiatric Association, 1994 [4], 2000 [5]) provides the official diagnoses for use in clinical practice, insurance company reimbursements, basic research, and the FDA approval of drugs. Nearly all the diagnoses are used for justifying the prescription of medications. of the 170 panel members who contributed to the two most recent editions of the manual, 56% had one or more associations with the pharmaceutical industry.

Most telling, if not chilling, 100% of the panel members involved in developing diagnoses for the categories of mood disorders and schizophrenia and other psychotic disorders had ties to drug companies. No wonder these diagnostic categories have become pharmaceutical company cash cows.

The most common ties among DSM panel members were through research funding (42%), consultancies (22%), and speakers’ bureaus (16%). This puts these professionals in much more intimate connection with their patent drug companies than merely accepting free lunches for the office staff or a free seminar.

Meanwhile, considerable criticism is being leveled at the degree to which major medical journals, including the hallowed New England Journal of Medicine, kowtow to the drug companies. Echoing criticisms I first made in Toxic Psychiatry in 1991, Richard Smith [81], former editor of the British Medical Journal for 25 years, wrote a 2005 analysis called “Medical Journals Are an Extension of the Marketing Arm of Pharmaceutical Companies”. Smith admitted, “Journal editors are becoming increasingly aware of how they are being manipulated, but I must confess that it took me almost a quarter of a century to wake up to what was happening.” He saw the problem as a combination of drug company-manipulated trials and the failure of journals, dependent on drug company advertising, to do their task of properly evaluating the papers sent in to them. As a former editor of the New England Journal of Medicine, Marcia Angell (2004 [7], 2007 [6]) even more vigorously lambasted the journals, including her own former journal, for its willingness to promote pharmaceutical industry interests.

Abramson and Starfield (2005) [1] asked the right question in their article titled “The Effect of Conflict of Interest on Biomedical Research and Clinical Practice Guidelines: Can We Trust the Evidence in Evidence-Based Medicine?” Their answer is no. In reality, so-called evidence-based medicine is a concept largely owned by drug company advocates who are trying to compel the use of their patron’s products. Abramson and Starfield referred to a British House of Commons report that found that “approximately 75% of clinical trials published in The Lancet, the New England Journal of Medicine (NEJM) and the Journal of the American Medical Association (JAMA) are industry funded”. Abramson and Starfield found that commercially funded studies are 5.3 times more likely to support their sponsors’ products than noncommercially funded studies. They concluded with a point I have been emphasizing for many years:

“So what are dedicated clinicians to do? The first step is to give up the illusion that the primary purpose of modern medical research is to improve Americans’ health most effectively and efficiently. In our opinion, the primary purpose of commercially funded clinical research is to maximize financial return on investment, not health.”
actually deteriorate as a result of taking these drugs (chapter 6).

**14.2.2 Eli Lilly Successfully Bamboozles the Legal System**

Many of my initial revelations about Eli Lilly and its drug Prozac in the earlier edition of this book were generated through my work as a medical expert in the first product liability case to go to trial against Eli Lilly concerning Prozac (Fentress, 1994 [40]; see Breggin, 1994 [21], for my testimony; see also Breggin, in press, for more details). In that case, Joseph Wesbecker entered his former place of employment in 1989, shot 20 people, killing 8 of them, and then committed suicide. He had been taking Prozac as well as other medications. The plaintiffs argued that Eli Lilly had failed to adequately study and then to warn physicians about the potential for Prozac-induced violence toward self and others.

Although the Wesbecker case was seemingly won by Eli Lilly by a divided 9-3 jury vote, the presiding judge, John W. Potter, later concluded that Eli Lilly settled secretly with the plaintiffs before the case went to the jury (Castellano, 1995 [27]; Gibeaut, 1996 [45]; Potter, 1995 [67]; Scanlon, 1995 [74]; most extensively, Varchaver, 1995 [85]). The judge had not been informed of the settlement during the trial. To the contrary, both sides denied its existence to the judge (Varchaver, 1995 [85]).

As a part of the settlement, in addition to receiving money and agreeing not to appeal the case, the plaintiffs agreed to withhold from the jury certain damaging evidence against Eli Lilly (Gibeaut, 1996 [45]; Potter, 1995 [67]; and others in the previous paragraph). Meanwhile, the trial went on as if no special arrangements had been made. This created a mock or fake trial.

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2One more vote against Lilly and it would have been a hung jury.

**14.1. RELYING ON JUNK SCIENCE**

people [like me] who have been inside the drug companies who
can tell you what is happening inside the drug companies. Of
course, you have avoided it."

“All the documents I am going to discuss now are on my
Web site, www.breggin.com. They have all been given to you
or sent to you via the FDA Committee.”

I went on to describe how one drug company, Eli Lilly, had falsified,
hidden, and manipulated data concerning Prozac-induced suicidal
behavior in adults. The FDA paid no attention and instead blithely
relied on the integrity of the data given to it by the drug companies
to whom so many of the panel members owned fealty.

The public is beginning to catch on to the untrustworthiness of
drug company data provided to the FDA and the medical
community. A recent editorial in USA Today titled “Drug Thugs” (2007)
[34] described pharmaceutical company harassment of medical critics,
something I am personally very familiar with. After discussing various
remedies, it made suggestions consistent with what I have been saying
for decades:

“Another approach would be to insist that the FDA do a
better job monitoring and publicizing studies conducted by the
drug companies themselves.”

“More transparency would make it harder for drug com-
panies to distort results. It would help to protect academic
freedom at America’s research institutions. And it would make
patients more likely to receive the safest and most appropriate
treatments.”

This chapter once again presents evidence that drug companies
cannot be relied on to present valid data about their drugs to the FDA,
the medical profession, or the public, and instead, that they underes-
timate the risks and overinflate the benefits of their products.
The focus is on Eli Lilly, the manufacturer of Prozac, and on GlaxoSmithKline, the manufacturer of Paxil. I cannot say with certainty that these companies are any more negligent than others; they are simply the companies I have learned the most about as a result of my independent research and my work as a medical expert in product liability suits against them.

14.2 Eli Lilly and Prozac

14.2.1 Eli Lilly Knew From the Start that Prozac Acts Like a Stimulant

After all the data had been collected during Prozac’s new drug application (NDA)\(^1\) approval process, FDA psychiatrist Richard Kapit (1986b)\(^[39]\), wrote the official safety review of adverse reactions or side effects. Kapit summarized, “Most frequently this new drug caused nausea, insomnia, and nervousness, which resembles the profile of a stimulant rather than a sedative drug.” He thought this stimulant profile would “give rise to the greatest clinical liabilities in the use of this medication,” including “insomnia, nervousness, anorexia, and weight loss”. Later in his report, Kapit repeated his observations, stating that Prozac’s “profile of adverse effects more closely resembles that of a stimulant drug than one that causes sedation and gain of weight”. Kapit concluded:

> “It is possible that these adverse effects of fluoxetine treatment may negatively affect patients with depression. Since depressed patients frequently suffer from insomnia, nervousness, anorexia, and weight loss, it is possible that fluoxetine treatment might, at least temporarily, make their illness worse.”

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\(^1\)NDA is the manufacturer’s basic documentation for the FDA in support of marketing the drug (see chapter 27).

Kapit repeated this concern in his summary, stating, “It is possible, therefore that fluoxetine may exacerbate certain depressive symptoms and signs.” He recommended that the label warn physicians about these dangers.

Later, in his safety update of the NDA on October 17, 1986\([51]\), Kapit spoke of several cases of a “syndrome of fluoxetine-induced hyper-arousal and excessive stimulation … [that] resemble episodes of stimulant drug intoxication”. It was especially likely to occur at higher doses, but it could occur at the standard 20 mgs. The state of overstimulation included “anxiety, agitation, insomnia, headache, confusion, dizziness, obtundation [mental clouding], memory dysfunction, tremor, impaired motor coordination Hyperactivity, hypomania, and mania may sometimes occur”. In overdose, the drug produces an even more flagrant stimulant syndrome culminating in seizures. Thus there is a continuum of stimulation effects.

Showing concern for possible abuse potential that might show up in the future, Kapit (1986c\([50]\)) warned about “the fact that fluoxetine causes a set of adverse effects which resemble those caused by amphetamine” (p. 23).

Despite Kapit’s function as the chief safety investigator for Prozac, the Division of Psychopharmacological Drug Products, under psychiatrist Paul Leber (see chapter 13), allowed none of Kapit’s concerns to appear on the drug’s label. The label does not indicate that Prozac is a potentially stimulant drug or that it can cause or worsen depression.

In a December 10, 1987, “Review and Evaluation,” Kapit\([50]\) recommended that the company conduct postmarketing tests to study Prozac’s potential to worsen the condition of patients already suffering from weight loss, anorexia, and agitation. Neither the FDA nor the manufacturer followed up on this.

It would take the FDA nearly two decades to finalize a new label for Prozac and all the newer antidepressants warning that patients can
especially if thwarted in his or her own ambitions of the moment. The increased rates on Prozac once again confirm its stimulant quality.

14.2.5 Eli Lilly Confirms and Hides Prozac Overstimulation

Pressured by the German drug regulatory agency, Eli Lilly asked Charles Beasley, from its Division of Clinical Neurosciences, to count the cases of agitation in their clinical trials (Breggin, 1994 [21]). He produced a secret in-house report titled “Activation and Sedation in Fluoxetine Clinical Studies” (Fentress Trial Exhibit 70; available on http://www.breggin.com), dated November 8, 1988. The report found that 333 Prozac patients became agitated in the trials, but only 16 placebo patients did so. Beasley called it an activation effect, including “nervousness, anxiety, agitation, insomnia”. He found that 38% of patients developed this effect on Prozac, and 19% developed it on placebo.

As mentioned in chapter 6, the totals for Prozac stimulation should have been even higher, however, because Beasley did not count several categories of overstimulation, including euphoria, mania, and hyperactivity. The rates of agitation would also have been higher if a large percentage of the Prozac patients had not been prescribed concomitant benzodiazepines and other sedatives.

In going through mountains of documents, I found no evidence that the FDA ever saw the crucial Beasley study that confirmed FDA investigator Kapit’s frequently expressed concerns about the drug’s similarity to stimulants, including amphetamine (e.g., Kapit, 1986c [50]).

When he found out that the case had been secretly settled and that the plaintiff and defense attorneys had lied to him, Judge Potter tried to amend the official outcome of the case from dismissed by the jury without prejudice to settled with prejudice. The judge’s attorney stated, “There was a payment of money to withhold evidence” (Wolfe, 1995 [86]). Initially, an appeals court overruled Judge Potter on the grounds that too much time had elapsed before his attempt to change the verdict (Varchaver, 1995 [85]; Wolfe, 1995 [86]), but the judge won his appeal to the Supreme Court of Kentucky (Gibeaut, 1996 [45]).

On May 23, 1996 [67], the Supreme Court of Kentucky unanimously agreed in Potter v. Eli Lilly & Co. that Judge Potter could proceed to hold a hearing on the secret settlement under an inherent-powers doctrine allowing courts to protect the integrity of their procedures (Gibeaut, 1996 [45]). The Supreme Court justices wrote, “In this case, there was a serious lack of candor with the trial court and there may have been deception, bad faith conduct, abuse of judicial process or perhaps even fraud” (“Trial Court’s Authority . . .”, 1996, p. 35; Gibeaut, 1996, p. 18 [45]).

Estimates of the secret settlement made by Eli Lilly and Company in the Wesbecker case have come through unrelated divorce suits. One plaintiff’s attorney, presumably privy to the Eli Lilly settlement amount and involved in his client’s divorce suit, stated, “The amount boggles the mind” (Gibeaut, 1996, p. 18 [45]).

Not only was the Wesbecker case settled secretly during the trial, but he plaintiffs lead attorney Paul Smith decided to settle all of his several other cases against Eli Lilly at that time. Eli Lilly can no longer claim it has never settled a Prozac case. It has settled several of them involving different attorneys.
14.2.3 Eli Lilly Acknowledges to the Food and Drug Administration (FDA) That Prozac Frequently Causes Depression

In preparing my testimony in the Wesbecker case, I went through an additional mass of FDA documents obtained under the Freedom of Information Act (FOIA). I discovered a section of Eli Lilly’s final draft of its Prozac label that was submitted to the FDA. The section, in conformity with the standard label, was titled “Other Events Observed During the Premarketing Evaluation of Prozac” (Eli Lilly, n.d. 36). It drew on the total database of 5,600 patients given Prozac. The label noted, “It is important to emphasize that, although the events reported did occur during treatment with Prozac, they were not necessarily caused by it.”

In this final version of their label, under the heading Nervous System, the company listed depression as a frequent adverse effect of the drug. Frequent is equivalent to common and means occurring at least once in 100 cases. But the FDA, supposedly in a last-ditch editing attempt to shorten what it called Eli Lilly’s laundry list concept, scratched a line through depression (Temple, 1987 383). The approved and current label lists only abnormal dreams and agitation as frequent or common. Depression went from being listed as a frequent adverse effect in the proposed official label to being wholly unmentioned in the final, approved label. This transformation took place at the very last minute, before the FDA’s final oval of the drug for marketing.

The admission that the drug was frequently reported to cause both agitation and depression is consistent with Richard Kapit’s original observations and is of great importance. Through research, clinical experience, and consulting as a medical expert, I have learned that many of the murders and suicides reported to have occurred during Prozac treatment seemed driven by a combination of agitation and depression, specifically, Prozac-induced agitated depression (Breggin, in press; Breggin et al., 1994a 26).

As a result, for more than a decade there was nothing in the Prozac label, or the label for any other antidepressant, indicating that the newer antidepressants can cause depression. Therefore, when a patient on Prozac became more depressed, rather than less, the physician was likely to increase the dose, rather than to stop or taper the drug. Only with the label revisions of 2004-2005 (chapter 28) did the FDA finally alert the profession to the fact that antidepressants can in fact make patients more depressed and worsen their overall condition. Unfortunately, the information has taken so long to surface that most physicians are habituated to the idea that antidepressants cannot cause depression.

14.2.4 Eli Lilly Hides the Implications of Prozac-Induced Mania

Even in the short clinical trials for the NDA, Prozac caused mania in slightly more than 1% of patients (Kapit, 1986c 50). But material that I turned up in the NDA indicates that Prozac poses a considerably greater danger of causing mania than the tricyclic antidepressants (Kapit, 1986c). In studies used for FDA approval, only 0.3% of patients on tricyclics became manic - a rate one-third that of Prozac. In addition, all the patients who became manic on tricyclics turned out to have a prior history of mania. Among the 33 reported cases of mania on Prozac, 23 occurred in patients who had never been manic before.

Mania frequently results in very destructive behavior toward oneself or others, including outright violence (chapter 6; Breggin et al., 1994a 26; especially Breggin, in press). Untold numbers of lives have been ruined by antidepressant-induced mania. The manic person can experience intense paranoid feelings and often feels enormous hostility,
Futhermore, the removal of several of the Prozac suicide attempt reports was wholly unjustified even in hindsight. For example, one discarded case involved a patient who took 10 fluoxetine capsules spaced at 2-hour intervals over 5 hours while drinking a bottle of rum. Taking the pills slowly in this manner, along with alcohol, is done during genuine suicide attempts to avoid vomiting the medication. The complete data on another exclusion was as follows: “The patient had suicidal ideation at the beginning of the study and made a self-inflicted laceration of the skin with a razor blade.”

In throwing out these cases, the Lilly consultants second-guessed the company’s own clinical investigators, who had originally categorized these reactions as drug-related suicide attempts during the double blind placebo-controlled clinical trials. In fact, this is highly unscientific and highly unethical because it undermines the entire concept of the double-blind study. The purpose of the double blind is to prevent exactly this kind of biased reanalysis of the data. Furthermore, the consultants made their decisions on their own personal impressions based on a mere few lines of clinical description. According to one of the company’s executives, they did not contact the authors of the reports - their own clinical investigators - for more information (Beasley, 1994a [10], p. 245). Yet these clinical investigators, based on firsthand knowledge, had cited the cases as suicide attempts.

The blinded data was the only valid data. However, Eli Lilly ran roughshod over science by breaking the blind in providing its new evaluators data indicating what each of the patients were taking when they were found to have attempted suicide. Thus, when “evidence-based” data did not meet the company’s need to promote its product, the company simply ignored the evidence and hired biased investigators to reevaluate the data while knowing which patients were taking Prozac and which were not. Eli Lilly’s own consultant, biological psychiatrist David Winokur, offered an explanation for how Prozac could increase the suicide attempt rate: “A possibility which comes to mind

14.2.6 Hiding the Risk of Prozac-Induced Mania and Aggression in Children

Clinical Psychiatry News (Sherman, 1995 [78]) headlined “Prozac for Kids: ‘Landmark’ Study Affirms Drug’s Use”. It described a placebo-controlled clinical trial led by Graham Emslie [38] from the University of Texas Southwestern Medical School in Dallas. When I evaluated the data from the newspaper report, the rate of drug-induced mania turned out to be an extraordinary 6% (Breggin, 1995 [22]). In addition, during the question period after the article was presented, Emslie admitted to an increase in aggressiveness as well (Sherman, 1995 [78]). When the article was later published, the extraordinarily important 6% mania rate was buried in a section devoted to dropouts (p. 1003) and left out of the abstract, discussion, and summary (Emslie et al., 1997 [31]). The increase in aggression was wholly unmentioned. The research was supported by Eli Lilly.

14.2.7 Eli Lilly and the FDA Ignore Reports of Aggressive Behavior on Prozac

As I described in Talking Back to Prozac (Breggin et al., 1994a [26]), the FDA made a presentation at its 1991 hearings on antidepressants and abnormal behavior that showed a disproportionately high frequency of reports to the FDA of hostility and intentional injury on Prozac compared to trazodone, an older and less-stimulating drug. (The graph, titled “Hostility and Intentional Injury: Reports per Million Rx,” Food and Drug Administration [FDA], 1991 [42], is available on http://www.breggin.com.) The graph and accompanying data show that in 1998, the first year that Prozac was marketed in the United States - and before there was any publicity surrounding Prozac-induced violence - there were approximately 10 times as many reports of violence and intentional injury per prescription for Prozac compared
to trazodone. By July 1991, reports of violence and intentional injury for Prozac became roughly 50 times more frequent per prescription than for trazodone.

The reports were sent to the FDA through its postmarketing spontaneous reporting system (SRS). The FDA representative projected the data onto a screen, but the data were not included in the transcript of the meeting. Although this issue was of overriding, central importance to its deliberations, the FDA advisory panel made no response at all to it. It was as if the data, so critical to their conclusions, had been presented to an empty room.

In response to a FOIA request from me, the FDA claimed that the data could no longer be found. I contacted the author of the graph, and he, too, told me that the data were lost. However, Eli Lilly was compelled to produce the data under court order in the Wesbecker case (Trial Exhibit 120), and I used it in my court testimony (Breggin, 1994 [21]).

As emphasized in chapter 7, the data once again confirm the importance of the spontaneous reporting system compared to controlled clinical trials in revealing dangerous adverse drug reactions, in this case violence and aggression.

### 14.2.8 Eli Lilly and the FDA Ignore Reports of Suicidal Behavior on Prozac

Another graph developed by the FDA for the 1991 hearing that compared Prozac to trazodone was called “Suicide Attempt, Overdose, and Psychotic Depression, Reports per Million Rxs” (available on http://www.breggin.com). Once again, these reports were far more common for Prozac. Beginning in 1988, the reports in this cluster for suicide, overdose, and depression were 4 times more frequent per prescription of Prozac. By 1990, they appeared to be approximately 50 times more common. The panel, which was rampant with conflicts of interest (Breggin et al., 1994a [26]), gave little importance to these findings.

### 14.2.9 Eli Lilly Hides Increased Suicidality on Prozac in Controlled Clinical Trials

In materials gained through discovery in the Wesbecker case, I found inhouse documents from Eli Lilly clearly demonstrating an increased rate of suicide attempts in Prozac patients compared to placebo and to tricyclic antidepressants (Breggin, 1994 [21]; available on http://www.breggin.com). This was a shocking discovery as Eli Lilly claimed, and continues to claim, that no such data exist.

In the summer of 1985, Eli Lilly set out to respond to accusations, including those from the German regulatory agency, that Prozac could cause or contribute to suicidality. The company evaluated data from its basic 4- to 6-week controlled clinical trials. Twelve reported suicide attempts were found among the Prozac patients, but only one each in the placebo group and the comparison drug group (tricyclic antidepressant). This 12:1 ratio could not be explained by differences in size between the Prozac group and the placebo and the tricyclic groups. When the total patient days of exposure were taken into account, the ratio remained a significant 6:1 for increased suicide attempts in the Prozac group.

Consultants hired by Eli Lilly pruned down the original reports, excluding six of the suicide attempts on Prozac and one on either the comparison drug or placebo. That is, they decided to throw out a substantial portion of the data that reflected badly on their employer’s drug. The ratio remained 6:1, and the consultants continued to find a borderline statistically significant \((p = .051)\) increased rate for suicide attempts among the Prozac patients.
It should be emphasized, however, that giving tranquilizers or sedatives along with Prozac by no means guarantees that the patient will escape undergoing drug-induced agitation, depression, suicide, or violence. The benzodiazepines can have paradoxical effects, including agitation. They, too, can cause or aggravate depression, violence, and suicide (chapter 13). Many of the most bizarre adverse reactions in my clinical experience occurred on a combination of SSRI antidepressants and tranquilizers, especially Xanax. In general, the greater the number of psychoactive drugs the patient takes, the greater the risk of an adverse drug reaction.

14.2.12 Prozac-Induced Aggression in Eli Lilly’s Earliest Animal Studies

In preparing for the Wesbecker trial, I found more evidence than I originally suspected concerning Prozac-induced agitation and even violence in animals. I testified at trial (Breggin, 1994 [21]) concerning an Eli Lilly animal study documented by Brophy, an Eli Lilly project leader. He reported, “A total of six dogs, two males and four females, from the high-dose group were removed from treatment for periods of 1 to 17 days due to severe occurrences of either aggressive behavior, ataxia, or anorexia.” In his deposition, Ray Fuller (1994) [44], Eli Lilly’s highest ranking scientist, stated that 6 of 20 dogs in the high-dose study group became unexpectedly aggressive. A number of mice were getting hyperactive, but not aggressive, on Prozac.

Slater et al. [80], from the Eli Lilly Research Labs, published an article in 1978 concerning the inhibition of REM sleep in cats. Disruption of REM sleep can cause emotional disturbances. The Eli Lilly researchers reported that they were “at a loss to explain why cats receiving fluoxetine for several days begin to hiss and growl or why this behavior decreased with continued treatment”.

is that Prozac might be somewhat more stimulating as a drug and that individuals may be slightly more impulsive although their thinking had not changed” (Breggin, 1994 [21], pp. 3129-3130; available on http://www.breggin.com). Independently, in my writing and testimony, I had also developed the concept of Prozac as a stimulating drug causing impulsive behavior and suicide.

As far as I can ascertain, these extremely important facts and analyses about Prozac-induced suicidality were never submitted to the FDA or in any way made available to the government, the profession, or the public. To the contrary, Eli Lilly has maintained — and continues to maintain — that there is no evidence whatsoever for increased suicidality on Prozac. As an example, Eli Lilly did not make known its analysis of increased suicidality on Prozac at the 1991 FDA conference (FDA, 1991 [42]). Nor did they present the Beasley data on increased activation (Beasley, 1988 [12]; as for all documents in this section, available on www.breggin.com).

14.2.10 Eli Lilly Employees Express Shame

Eli Lilly’s successful attempts to hide suicide attempts by miscoding them resulted in expressions of shame and guilt within the company. On November 13, 1990, Eli Lilly employee Claude Bouchy (1990a [18]; available on www.breggin.com) wrote a memo to Leigh Thompson, a high-ranking U.S. administrator in the company, and to five other company officials showing his concern about how the company was identifying or coding adverse drug events that physicians were reporting to the company. He protested the requirement for safety staff to change reports of suicide attempts to reports of overdoses and to change reports of suicidal ideation to depression. Bouchy spoke of another employee who also had “medical problems with these directions” and said, “I have grave concerns about it”. Bouchy wrote:
"I do not think I could explain to the BGA [the German drug regulatory agency], a judge, to a reporter or even to my family why we would do this especially on the sensitive issue of suicide and suicide ideation."

Bouchy then went on to say that the issue had been "argued back and forth for about a month" between Germany and Indianapolis, Lilly's home office, and that "therefore I am bringing it to your attention and await your directions".

One day later, on November 14, 1990, Bouchy again wrote from Germany to Leigh Thompson with copies to five other company officials, describing how Lilly was purposely hiding Prozac-induced suicidal ideation and acts under false and misleading categories. This time Bouchy (1990b) [17] wrote:

"Finally, on a very simple and non-scientific basis, I personally wonder whether we are really helping the credibility of an excellent ADE [adverse drug event] system by calling overdose what a physician reports as suicide attempt and by calling depression what a physician is reporting as suicide ideation. Of course by the end of the day we will do what we are told to do but Hans and I felt that we had to bring these to attention."

The FDA creates a list of preferred terms to be used to describe specific adverse drug reactions. By January 1989, the year before these memos were written, FDA's dictionary, called COSTART, clearly specified that suicide attempts should be listed as suicide attempts (available on http://www.breggin.com). But regardless of the FDA dictionary, Eli Lilly was clearly trying to hide suicidal thoughts and suicide attempts under more obscure categories.

Eli Lilly not only excluded suicide attempts from the list of adverse drug reactions by calling them depression or even failure to improve (Breggin et al., 1994a [26]), the company instructed its principal investigators not to report possible adverse drug events from the controlled clinical trials if they could be attributed to the patient’s mental disorder (Beasley, 1994b [11]), further discouraging them from sending in reports of suicide attempts in depressed patients.

14.2.11 Adverse Reactions to Prozac in Eli Lilly’s Earliest Research

In the March 1986 safety review of the NDA (Kapit, 1986b [49]), the FDA psychiatrist summarized five “serious clinical events” in the first 77 patients given Prozac, including 1 with paranoid psychosis and 1 with manic psychosis. There was also evidence in Eli Lilly’s files presented in my testimony that some of the first human subjects responded very adversely to Prozac. In his deposition, Eli Lilly’s top scientist, Ray Fuller (1994) [44], confirmed the existence of an early in-house memo, in which he wrote:

"Some patients have converted from severe depression to agitation within a few days. In one case the agitation was marked and the patient had to be taken off the drug. In future studies, the use of benzodiazepines to control agitation will be permitted."

This is a smoking gun, indicating that Eli Lilly knew from the beginning that Prozac would make many patients so agitated that they would need other drugs to control it. Fuller (1994) [44] admitted in deposition that the decision was made to add benzodiazepines to the NDA clinical studies because patients reportedly were becoming agitated on Prozac. As noted, the use of concomitant sedatives and minor tranquilizers became a common practice in the protocols preceding drug approval.
Akathisia can contribute to the development of psychosis as well as violence against self or others. Dystonia often produces agonizing muscle spasms in the region of the eyes, head, and neck but can also cause spasms that disable the whole body. Parkinsonism produces emotional dulling and immobilizes the body.

The original 1989 Prozac label, under the heading “Adverse Reactions of the Nervous System,” mentions akathisia as infrequent. However, in the September 1989 issue of the Journal of Clinical Psychiatry, Joseph Lipinski et al. from McLean Hospital and Harvard Medical School described five cases of Prozac-induced akathisia, which they believed occurred “fairly frequently”. They estimated the rate of akathisia in Prozac patients at between 9.7% and 25%. They stated that their cases were indistinguishable from neuroleptic-induced akathisia. In a case example, 5 days after starting Prozac, one woman “reported severe anxiety and restlessness. She paced the floor throughout the day, found sleep at night difficult because of the restlessness, and constantly shifted her legs when seated”.

One year later, in June 1990, Health Letter (Public Citizen’s Health Research Group, 1990) estimated that akathisia affects a whopping 15% to 25% of Prozac patients.

How could such a frequent, distressing side effect go almost wholly unrecognized among the thousands of patients tested by Eli Lilly during the FDA drug approval process? In reviewing documents for product liability suits against Eli Lilly, I found that the company had not listed akathisia as one of the preferred terms for use in describing adverse effects in its clinical trials. That is, their researchers were not given the term akathisia as one of the categories or terms for reporting effects. As a result, few reports of akathisia cropped up. Instead, cases of akathisia were listed under more innocuous terms like hyperactivity or agitation, drug-induced symptoms not as closely associated with suicidality, violence, and overall mental deterioration as akathisia.

In defense of their company and their drug, these authors then explained, “The subjects who received fluoxetine in Phase I clinical trial have not described any change in mood nor have observers noted any change in affect.” This claim is not supported by the facts as disclosed in the NDA or in Eli Lilly’s own documents. As the previous section documented, some of the first subjects given Prozac showed drastic, even deteriorating changes.

I can find no evidence that follow-up studies were done to further evaluate Prozac-induced agitation or aggression in animals. No primates were tested for behavioral effects.

14.2.13 British and German Regulatory Authorities Inquire About Prozac-Induced Stimulation, Agitation, and Depression

The FDA was not the only regulatory agency to show concern about Prozac-induced agitation, stimulation, and depression. In my Wesbecker testimony, I described how the British Committee on Safety of Medicines (CSM; as cited in Breggin, 1994) prior to approval of Prozac, raised the same issue:

“It is possible that these adverse effects of fluoxetine treatment may negatively affect patients with depression. Since depressed patients frequently suffer from insomnia, nervousness, anorexia and weight loss [Prozac effects], it is possible that fluoxetine might at least temporarily make their illness worse.” (p. 3094)

For a time, the CSM seemed determined to make Prozac contraindicated in underweight, anorexic, or agitated patients, but apparently, nothing came of it.

We must also doubt Lilly’s methods of selecting Phase 1 subjects (see subsequent discussion).
During the mid-1980s, the German Drug Regulatory Agency (BGA; Bundesgesundheitsamt) also raised doubts about approving Prozac. The agency worried about a possible increase in the suicide rate. They shared Kapit's concern about stimulating effects. (Consistent with my own impressions, the BGA also found that doctors in clinical studies were more positive about the drug than the actual patients.)

In 1984, Eli Lilly employees in Germany named Schenk and Weber (as cited in Breggin, 1994 [21]) wrote in a company memo, “The BGA suspects fluoxetine to be a stimulating/activating drug (side-effect profile, suicides, suicide attempts)” (p. 3151). Remarkable on suicide associated with Prozac, they declared, “This is a very serious issue in the opinion of the BGA.” According to the memo, the BGA had stated, “Considering the benefit and the risk we think this preparation totally unsuitable for the treatment of depression.” The BGA was especially concerned about Prozac’s potential to cause agitation before its antidepressant effect took place. The BGA, unknowingly echoing Kapit, but more strongly, warned, “During treatment with the drug, some symptoms of the underlying disease (anxiety, insomnia, agitation) increase, which as adverse effects exceed those which are considered acceptable by medical standards.”

The conflict between the BGA and Eli Lilly went on for many years. On February 6, 1991, Hans Weber, representing Eli Lilly in Germany, wrote to Ray Fuller at Eli Lilly. He described a meeting held between Eli Lilly representatives and the BGA. Weber (as cited in Breggin, 1994 [21]) stated, “The question was raised whether fluoxetine could be an amphetamine-like drug, which may explain its stimulating and anorectic effects” (p. 3154).

Eventually, the BGA did approve Prozac. Unlike the FDA, however, they required a label warning under the heading Risk of Suicide. It states that the patient may need an additional sedative along with Prozac until the antidepressant effect takes over. It notes that this would also apply to patients with extreme sleep disturbances or ex-Itability.

Lilly’s undisclosed in-house studies of increased activation and suicidality on Prozac were probably done in the hope of allaying fears expressed in Germany and elsewhere. When the studies instead confirmed the worst fears about stimulation and suicidality, they were never made known to the relevant agencies in England, Germany, or the United States.

### 14.3 Eli Lilly Hides Akathisia

As early as 1979, Meltzer [62] and a team at the University of Chicago recognized that Prozac suppresses dopaminergic neurotransmission. Concerned about reports of neurological side effects that might stem from this dopamine suppression, Baldessarini and Marsh (1990) [8] from McLean Hospital and Harvard demonstrated the effect in Prozac-treated animal brains.

Drug-induced disruption of dopamine neurotransmission is known to produce a variety of neurological side effects (see chapters 12 and 29). The neuroleptics suppress dopamine neurotransmission, causing a reactive hyperactivity of the system that produces a high rate of irreversible dyskinesias, cognitive dysfunction, and dementia.

Prozac’s pharmacological mechanism for suppressing dopamine is more indirect than that of the neuroleptics. However, the clinical result can be very similar. Prozac can cause akathisia (agitation with hyperactivity), parkinsonism (“Fluoxetine,” 1990), and dystonia (muscle spasm) (Meltzer et al., 1979 [62]; Reccoppa et al., 1990 [71]).

Drug-induced akathisia, dystonia, and parkinsonism can produce extreme discomfort. They can be disabling and feel-like torture (see chapter 3 for details). In brief, akathisia can become an inner torment and anguish that drives the individual into hyperactivity.
14.8 Eli Lilly Mired in Controversies with Life-Threatening Implications

Many other controversies involving Eli Lilly and Company, the maker of Prozac, have raised further questions concerning pharmaceutical industry adherence to ethical practices and FDA standards. The media and the FDA have investigated Eli Lilly’s use of homeless alcoholics as normal experimental subjects in Phase I studies (Cohen, 1996 [28]; “NIH Queries University,” 1996 [65]). This is not an acceptable practice, according to the FDA. Because homeless, addicted people might feel compelled by the offer of large sums of money and a safe place to stay, they are not capable of freely consenting to experiments. The use of homeless, alcoholic people could also compromise the research results. Confused by their preexisting drug problems, they might fail to detect adverse reactions to the experimental drug. They might also be unwilling to report adverse effects for fear of being dropped from the study and left penniless and back on the streets.

An advertising campaign by Eli Lilly has raised the specter of unleashing more widespread adverse drug reactions on the public before these dangers can be detected or appreciated by doctors. Writing in The Wall Street Journal, physician Philip R. Alper (1996) [2], asked, “Who to Trust: Drug Companies or Your Doctor?” Alper criticized Eli Lilly’s promotion of a new, expensive form of insulin, Humalog, directly to the public through two-page ads in People magazine. The aim of these “market blitzes,” according to Alper, “is to create consumer demand even before the doctor would be willing to use the drug spontaneously. Call it an end-run around the doctor, arm-twisting, manipulation, or whatever. The result is the same”. These promotional tactics, Alper warned, will cause patients to press doctors to prescribe new drugs before their safety has been sufficiently demonstrated.

14.4 Lilly Covers Up Prozac Withdrawal Reactions

Withdrawal from SSRIs, Effexor, and the newer antidepressants can be difficult and sometimes impossible and can involve a broad range of symptoms (chapter 5). Patients can crash coming off SSRIs and Effexor and undergo severe depression and suicidal ideation (Breggin, 1992b [20]; Breggin et al., 1994a [26]). Here I want to emphasize that Eli Lilly knew about withdrawal problems from Prozac but hid them from the profession and the public. Einbinder (1995) [35] described a patient who felt fatigue and dizziness with falling on withdrawing from Prozac. Interestingly, Einbinder stated, “The manufacturer was unaware of any reports of withdrawal symptoms on cessation of fluoxetine.”

It is most remarkable if Eli Lilly told Einbinder that it was unaware of any reports of withdrawal symptoms associated with the use of Prozac. By January 24, 1993, the SRS of the FDA had received 94 reports of withdrawal syndrome from Prozac as well as 26 reports of drug dependency and 4 of drug addiction (FDA, 1993 [43]).

I myself made a report in the literature on Prozac withdrawal (Breggin, 1992b [20]), and I sent it directly to the company as well. The company acknowledged receipt of the document (D. Marvel, personal letter, March 15, 1993) and filed it with the FDA using several event terms, including withdrawal syndrome.

There is no way that Eli Lilly could have been unaware of reports of withdrawal reactions from Prozac.

By the mid-1990s, there were also reports of severe withdrawal from Paxil and Zoloft. Debattista and Schatzberg (1995) [32] reported on physical symptoms associated with a case of paroxetine withdrawal with vomiting, headache, and tremulousness, which they compared to a similar report concerning sertraline withdrawal (Louie et al., 1994
58).

14.5 Similar Drug Approval Problems with Zoloft and Paxil

Through FOIA, I have had the opportunity to review the Zoloft Summary Basis of Approval (1988). Many of the problems that plagued the NDA of Prozac were also rampant in the NDA for Zoloft, including numerous violations of protocol, the use of concomitant long-acting benzodiazepines, high dropout rates, many negative studies, and no evidence of efficacy in hospitalized patients. In fact, the efficacy of Zoloft was considered questionable until the last minute before its final approval (discussed in chapter 3).

Through FOIA and materials obtained as an expert witness in product liability cases against GlaxoSmithKline, I found similar problems to Prozac in regard to the approval process for Paxil, especially mis-coding suicidal behavior as “emotional liability” and hiding or misinterpreting data on suicidality (see subsequent sections in this chapter).

14.6 Prozac Interaction with Monoamine Oxidase Inhibitors and Tryptophan

When combined with other drugs that stimulate the serotonergic system, such as monoamine oxidase inhibitors, other antidepressants, or tryptophan\(^4\), Prozac and the other SSRIs, as well as any antidepressant that blocks the removal of serotonin from the synapse, can produce a well-documented, severe condition called the serotonin syndrome (Sternbach, 1991\(^8\)). This disorder includes the usual signs of overstimulation, such as euphoria and hypomania, agitation, confusion, and gastrointestinal upset, including diarrhea. However, the serotonin syndrome additionally involves overstimulation of the brain stem and spinal cord, producing fever and chills, severe incoordination, muscle spasms, and hyperactive reflexes. It bears some similarity to neuroleptic malignant syndrome, and like NMS it can also be lethal (chapter 15).

14.7 Prozac in Combination with Tricyclic Antidepressants

Psychiatrists and other physicians too frequently combine Prozac with other antidepressants, including the tricyclics, such as imipramine (Tofranil) and amitriptyline (Elavil). The combination is extremely dangerous. In a 1992 study conducted in Eli Lilly’s own research laboratory by the team of Bergstromm et al.\(^16\), Prozac was found to increase the blood concentrations of tricyclics by as much as 10 times.

The tricyclics become toxic at blood levels not much higher than their therapeutic ones. A 10-fold or more increase in concentration of a tricyclic could produce, among other things, a fatal heart arrhythmia, a severe drop in blood pressure, CNS depression, or a grand mal seizure. It could also cause abnormal mental reactions such as confusion, panic, mania, or even depression.

One rat brain study showed that Prozac and tricyclics given together accelerate their joint impact on the brain (Baron et al., 1988\(^9\)). Downregulation of adrenergic receptors (discussed subsequently) was greatly increased in rapidity and intensity by the combination.

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\(^4\)The brain synthesizes serotonin from tryptophan, an essential amino acid found in a variety of foods. The ingestion of large amounts of tryptophan increases the production of serotonin.
Although Eli Lilly denies any wrongdoing whatsoever in the Zyprexa diabetes and pancreatitis cases, why would a company pay more than a billion dollars just to get the lawyers to drop false charges? That is hardly a nuisance settlement; it is a mammoth settlement. The answer lies in the part of the agreement that allows all of the incriminating documents to remain sealed.

Instead of trying to clear its name, and to conform with principles of transparency in business and medicine, Eli Lilly continues to fight for its right to hide itself beneath the dark mud of corporate secrecy. But in this case, the truth emerged (Creswell, 2006 [31]). Jim Gottstein, president of the Law Project for Psychiatric Rights (http://psychrights.org) in Alaska, obtained the sealed documents. He then released the documents to the public, including evidence that Eli Lilly pushed the drug for off-label (unapproved) uses and hid the risk of Zyprexa causing pathological weight gain and diabetes—accusations that the drug company has denied (Creswell, 2006 [31]). The sealed documents became the basis of a series of New York Times articles (Berenson, 2006a [15], b & c [13] & [14]; Creswell, 2006 [31]; “Playing the Risks,” 2006 [66]). In an editorial on December 19, 2006, The New York Times discussed Lilly’s hitherto secret documents and called for “congressional hearings that should focus on how well the industry complies with existing laws and how effectively the FDA regulates the industry’s marketing materials” (“Playing Down the Risks,” 2006 [66]).

Eli Lilly went to court to fight Jim Gottstein’s release of the documents and prevailed with the judge, who ordered them returned, but the documents were already sailing around the Internet. Writing in the Journal of the American Medical Association, physicians Aaron Kesselheim and Jerry Avorn (2007) [53] viewed this as one of a series of positive events demonstrating the need for greater transparency in

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14.8. ELI LILLY LIFE-THREATENING

Before drug companies advertised directly to the public, the introduction of drugs into the marketplace was more gradual and hence safer. Many prudent doctors would wait to observe the results with new drugs before prescribing them to their own patients, knowing that serious or life-threatening adverse effects might not be detected before the drug was widely prescribed.

Alper (1996) [2] expressed concern that Humalog and other drugs could meet the same fate as Eli Lilly’s earlier medication, Orarex, which, he says, was among the first to be promoted directly to the public. It caused fatalities and was taken off the market in 1982. Eli Lilly pleaded guilty to criminal charges in regard to Orarex (FDA, 1987a [41]; Shenon, 1985 [77]). Alper (1996) [2] lamented bygone days, when Eli Lilly was a “bastion of the ethical drug industry.” He attributed the problem to a general decay of ethical conduct within the pharmaceutical industry.

In another controversy, National Institutes of Health (NIH) researchers were conducting Phase I studies for a new Eli Lilly investigational drug called flururidin (FIAU), as a treatment for liver disease (“FDA Tightens,” 1994 [39]). The FDA accused Lilly of serious violations by failing to inform volunteers of all the risks and by failing to report severe drug reactions, including fatalities, until months, and even a year, afterward (“Hepatitis Drug,” 1994 [48]). An NIH panel attempted to defend the company and the institute from FDA accusations (Altman, 1994 [3]; Schwartz, 1994a [76]; Thompson, 1994 [84]). The FDA (1994; Schwartz, 1994b [75]) issued new proposed regulations that cited the failures of Eli Lilly in regard to its FIAU research.

Strattera (atomoxetine), the supposedly safer “nonstimulant” treatment for ADHD, turned out to be highly stimulating and is the only ADHD treatment required to carry a black-box warning, with a heading about how it can cause “Suicidal Ideation in Children and Adolescents” (chapter 13).
Lilly’s new antidepressant, Cymbalta ( duloxetine), was mired in controversy even before it was approved when a young woman committed suicide while taking the drug in a controlled clinical trial in which the drug was being tested for the treatment of stress urinary incontinence. Medical reporter Jeanne Lenzer (2005b) attempted to pursue the facts about this and other apparent deaths among patients taking duloxetine. Both Eli Lilly and the FDA stonewalled Lenzer on the grounds that duloxetine did not win approval for treating stress incontinence and therefore the information about that phase of its testing remained the private (and secret) property of Eli Lilly. Meanwhile, marketed as the antidepressant Cymbalta, duloxetine became another big moneymaking drug for the shrewd company. Once again, Eli Lilly put its financial interests ahead of science and public health.

Eli Lilly has a long history of minimizing the dangers of its products, resulting in unnecessary pain, suffering, and death. As an earlier example, several decades ago Eli Lilly began marketing Darvon (propoxyphene) as a relatively nonaddictive painkiller; but before long dependence and abuse became a problem of epidemic proportions. The controversy continues. The Public Citizen’s Health Research Group (2006) petitioned the the FDA to ban the drug on the grounds that there were over 10,000 “confirmed deaths” and 2,110 “accidental deaths” associated with the drug in the U.S. from 1981 through 1999. The analgesic is commonly prescribed in combination with the drug acetaminophen (Tylenol) as Darvocet and also as generic products.

Eli Lilly’s methadone, used in drug addiction clinics as a substitute for other narcotics, has also drawn a great deal of persistent worldwide criticism. It has been diverted for illegal use as a highly addictive narcotic. It has caused many deaths, including a “public health crisis that involved an unusual spike in methadone overdose deaths in the Portland area,” according to the Drug Enforcement Administration (2007).

Eager to take advantage of any drug-marketing niche that it can, Eli Lilly is often in the forefront of producing deadly chemical agents. This is nowhere more apparent than its attempts to hide the truth about its current big seller, Zyprexa.

14.9 Lilly Fights to Hide Data on Deadly Adverse Drug Effects

Eli Lilly promoted Zyprexa as an atypical, and hence relatively safe, antipsychotic drug. It published badly skewed research trying to show that Zyprexa was relatively free of the risk of causing tardive dyskinesia when in fact it was not (chapter 30). More shocking, Zyprexa and other so-called atypicals turned out to produce an especially lethal adverse effect: acute and chronic diabetes. Once again, the Lilly product seemed to be among the worst offenders and became the center of another controversy in which Eli Lilly fought and continues to fight to hide the incriminating data, while paying out huge sums of hush money.

On June 15, 2005, in a multistate product liability suit, Eli Lilly settled for $690 million. Most of the case involved life-threatening diabetes caused by Zyprexa. I was hired as a medical expert by Hersh and Hersh, a California law firm involved in that multisuit, multistate legal action, and had the opportunity to evaluate sometimes lethal cases of diabetes and pancreatitis caused by Zyprexa. Some cases became chronic; other patients died within hours of onset. My Web site (http://www.breggin.com) contains more details on the Eli Lilly settlement. Meanwhile, similar cases have continued to be brought with potential payouts, or settlements, by the company estimated at $1.2 billion (Rosack, 2007).
Mr. Farber responded by producing my extremely detailed report in the Lacuzong case to bolster my accusations of negligence. As a result of the additional evidence, the judge allowed the case against the company to go forward.

A couple of years later, I discovered that the Lacuzong report was now available to the public by the U.S. District Court for the Southern District of Mississippi. Inadvertently, the submission of the report in the new court turned it into a public document available to anyone who requested it through proper channels. When I discovered that this was possible, I asked attorney Derek Braslow to obtain a copy of my report from the court, and then I placed the complete report on my Web site (http://www.breggin.com). I also wrote a series of three articles for Ethical Human Psychology and Psychiatry reviewing and excerpting large portions of it (Breggin, 2006a [23], b&c [24] [25]).

While I was writing the three articles in 2006, the FDA was in the process of requiring the antidepressant manufacturers to reevaluate their controlled clinical trials in regard to the risk of antidepressant-induced suicide in adults - the subject of my Lacuzong report. Before the last of my three reports was published, in May 2006, GSK published a Dear Healthcare Provider letter documenting that its reevaluation of its own clinical trial data showed that Paxil increased suicidality in adults, including all ages of adults suffering from major depressive disorder.

An important issue in the Lacuzong case was the capacity of one, two, or three daily doses of Paxil 10 to cause severe mental disturbances. During my site visit to the offices of GSK, I combed through adverse drug reaction reports to determine how early in treatment they began. I discovered that the first few days were the greatest time of risk.

My analysis of GSK’s sealed documents confirmed that the company had hidden the true rate of suicidality by failing to report all drug testing.

14.10 Glaxosmithkline (GSK) and Paxil

14.10.1 Paxil Overstimulation

Overstimulation is a common problem with all SSRIs and most of the newer antidepressants. For Paxil, as in the Prozac studies, agitation and insomnia were among the reasons for the dropouts. As documented on its official label, Paxil displays a similar pattern of stimulant effects: insomnia, tremor, nervousness, and anxiety. Like Zoloft, it also produces more somnolence and more sexual dysfunction than Prozac. In fact, somnolence (23.3%) is almost twice as frequent as insomnia (13.3%).

For Paxil, the list of psychiatric disorders reported in association with drug treatment is categorized under nervous system. Again, the company makes the point that these reactions were reported but not necessarily causally related. As of the early 1990s, the data base included 4,126 patients. The list of frequently reported reactions includes, among others, central nervous system (CNS) stimulation, depression, and emotional lability. Chapter 4, table 7.1, lists many stimulant or stimulant-like adverse effects of Paxil summarized from the label, including hypomania/mania, euphoria, insomnia, nervousness, anxiety, agitation, hostility, psychosis, paranoid reaction, central nervous system stimulation, emotional lability, tremor, sweating, and palpitation.

Probably because Paxil is the most toxic and the most stimulating of the SSRI antidepressants, in recent years, I have been deluged with inquiries about cases of Paxil-induced mayhem, murder, and suicide (Breggin, in press). My experience is consistent with the FDA finding that among all of the antidepressants only Paxil, by itself and without
being pooled with the other antidepressants, caused a statistically significant increase in suicidality in adults across the age groups (chapter 11).

Most of my inside information concerning Paxil was accumulated in late 1999 and remains valid to this day. At that time, I was asked by California attorney Don Farber to be the medical expert in a product liability case that was brought by the family of Reynaldo Lacuzong in California against Paxil manufacturer GlaxoSmithKline (GSK).

### 14.10.2 The Lacuzong Case

Reynaldo Lacuzong\(^6\) drowned himself and his two small children in a bathtub. There was no evidence of any previous suicidality or violence on his part or of any animosity toward his children. He had never seen a psychiatrist, been to counseling, or displayed symptoms of psychiatric problems. For years, Reynaldo had received outstanding evaluations as an employee at a high-tech firm.

What had changed in his life? He was on the third day of taking Paxil 10 mg, the smallest available dose. It had been prescribed, most likely, to help him with the tension involved in giving up his customary one or two alcoholic beverages each evening.

Reynaldo quickly developed akathisia - agitation accompanied by a compulsive need to move- as well as other manic-like symptoms of irritability and anxiety. As described in chapters 4 and 31, antidepressant induced akathisia can cause violence, suicide, psychosis, and an overall worsening of the patient’s mental condition.

I became a medical expert in Reynaldo’s case and was authorized by the judge in the case to examine the enormous volume of sealed drug company files concerning Paxil contained in GSK’s record room. At-\(^6\)he section about the Lacuzong case draws on a similar section in my book Medication Madness (in press).

torney Don Farber and I, with the help of my assistant, Ian Goddard, devoted several days to examining the materials, including clinical trial data, adverse drug reaction reports and analyses, and tell tale correspondence between the drug company and the FDA.

My July 21, 2001, expert report in the Lacuzong case was very lengthy and detailed charges of negligent behavior on the part of GSK, including the drug company’s practices in developing and marketing Paxil and, in particular, its mishandling of information about the drug’s dangerousness in regard to producing violence and suicide.

The Lacuzong product liability case against GSK was eventually resolved to the satisfaction of the Lacuzong family. The company, of course, denied, and continues to deny, all of the allegations made against it in the lawsuit. The settlement amount was not disclosed, but Mr. Farber went from working out of his home to working in a private office and has become one of a handful of highly experienced attorneys in the arena of antidepressant litigation.

As a part of the settlement, GlaxoSmithKline was allowed to keep secret its records, and I was not allowed to make public my findings. Because my findings were of grave public health significance, including my discovery that the company had manipulated data to minimize the threat of Paxil-induced suicidality, Mr. Farber went to court to ask the judge to unseal the data, but the judge supported the company’s right to withhold its proprietary information.

A few years later, after the Lacuzong case had been resolved, I became a medical expert in another Paxil suicide case, and I urged the new attorney to bring in Mr. Farber as a consultant. My report in this new case was limited in scope by the fact that everything I had learned in the earlier Lacuzong case was sealed, apparently including my original report. After my report was given to the court, GSK asked the judge in the U.S. District Court for the Southern District of Mississippi to dismiss the case on the grounds of insufficient evidence.
consumers urgently needed the truth. It also made a mockery of the
need to protect America’s children from adverse drug effects.

Partly inspired by the disclosures in the Canadian medical journal
(see Sibbald, 2004 [70]) and events in Great Britain (see subsequent
sections), on June 2, 2004, the attorney general of New York State,
Eliot Spitzer, filed suit to force GSK to release its complete clinical
data on Paxil and children (People of the State of New York v.
GlaxoSmithKline, 2004; see also Office of New York State Atto-
ney General Eliot Spitzer, 2004). This most remarkable document
provided a detailed indictment of the drug company’s activities.

The Spitzer suit claimed, “GSK has engaged in repeated and per-
sistent fraud by misrepresenting, concealing and otherwise failing to
disclose to physicians information in its control concerning the safety and
effectiveness of its antidepressant medication paroxetine . . . in treating
children and adolescents with Major Depressive Disorder”.

The suit provided an analysis of efficacy in GSK’s trials, indicating
that the drug was often no better than placebo. In an analysis of
safety, it found that several combined studies showed that “possibly
suicide related behaviors were approximately two times more likely in
the paroxetine group than the placebo group”. It disclosed that in
five studies, “GSK coded suicidal thinking and acts, as well as mood
swings, crying and similar behaviors, as ‘emotional lability’.”

Spitzer’s report revealed that internal GSK documents discussed
how to spin negative studies into positive ones in an effort to “manage
the dissemination of these data”. As originally disclosed in the Cana-
dian Medical Association Journal, this management included publish-
ing a positive article about an essentially negative report (Study 329).

The suit alleged that GSK misrepresented the safety and efficacy
of Paxil for children and youth to its own sales force, falsely stating
“Paxil demonstrates remarkable Efficacy and Safety in the treatment
of adolescent depression.” This not only ignored withheld data but

suicide attempts on Paxil, by artificially inflating the number of sui-
cides for patients taking placebo, and - in a fashion similar to Eli
Lilly - by miscoding many suicides. The company had listed numer-
ous suicide attempts under the relatively benign category of emotional
lability (emotional instability), making it difficult, if not impossible,
to ever locate all of them.

Again like Eli Lilly, sealed company data also showed that the com-
pany systematically failed to report cases of akathisia and that some
of the suicide cases were related to that anguish-inducing drug reac-
tion. Again like Eli Lilly in regard to Prozac, the company disguised
the stimulating effects of Paxil by constructing different subcategories
for overstimulation, such as nervousness, anxiety, and hyperactivity,
without adding them up to show the high overall rates of stimulation.

My search of the company files also disclosed correspondence from
the FDA warning the drug company that its advertising and market-
ing practices were promoting an unfairly positive picture of the drug
in comparison to other antidepressants and ordering the company to
stop. All of these findings are documented in the series of three arti-
cles (Breggin, 2006a [23], b&d [24] & [25]) and in the LacuZong report
on my Web site.

14.11 Paxil and GSK Criticized By Medical
Journals and Foreign Drug Regulatory
Agencies

Although the last year or two has seen exceptions (e.g., Kesselheim et
al., 2007 [53]), it is rare indeed for medical journals to criticize drug
companies. The journals are well-heeled partners in the pharmaceu-
tical complex, deriving huge support from advertising. But the
actions of GSK were so outrageous that journals took notice, at least
in Canada and Great Britain.

On March 2, 2004, the Canadian Medical Association Journal reported on a 1998 internal GSK document that had been leaked to it (Kondro et al., 2004 [54]). The memorandum “advised staff at the international drug giant GlaxoSmithKline (GSK) to withhold clinical trial finds in 1998 that indicated the antidepressant paroxetine...had no beneficial effect in treating adolescents”.

The leaked position paper prepared by the Central Medical Affairs team, a division of the company, referred to the drug by both its U.K. (Seroxat) and North American (Paxil) names, indicating that it aimed at influencing both markets. It provided guidance on how to manage two clinical trials conducted by the company. According to the position paper, the clinical trial results were “insufficiently robust” to support an application to regulatory authorities for the use of the drug in treating pediatric depression. GSK’s Central Medical Affairs team recommended that the company “effectively manage the dissemination of these data in order to minimize any potential negative commercial impact”.

The GSK document addressed two studies: In Study 329, paroxetine was no more effective than placebo, and in Study 377, placebo was actually better than paroxetine. The Central Medical Affairs team then explained that Study 329 would be published as an abstract (summary), but “it would be unacceptable to include a statement that efficacy had not been demonstrated, as this would undermine the profile of paroxetine”.

Even worse, GSK made sure that Study 329 was eventually published in a whitewashed form in the prestigious Journal of the American Academy of Child and Adolescent Psychiatry (Keller et al., 2001 [52]). The title left no doubt about the scientific nature of the study: “Efficacy of Paroxetine in the Treatment of Adolescent Major Depression: A Randomized, Controlled Trial”. The conclusion to the lengthy analysis, a mere one sentence long, left no doubt about what the reader was supposed to learn: “Paroxetine is generally well tolerated and effective for major depression in adolescents”. That one sentence, so prominently displayed as the last line of the abstract, was a drug company public relations triumph, one bound to vastly increase the off-label prescription to children of their ineffective, dangerous drug.

With a list of 22 authors, many among the best known in the field, the GSK-engineered article is a living demonstration that America’s psychiatric drug experts serve as a stable of horses kept and run by the pharmaceutical industry. Collectively, they manufactured a powerful go-ahead signal to the medical profession to liberally prescribe Paxil off-label to children.

14.12 The Attorney General of New York State Takes Action Against GSK and Paxil

When a drug fails to get FDA approval for a particular indication, such as GSK’s Paxil for the treatment of depression in children, drug companies have exercised their proprietary right not to release information about the testing. In the case of Paxil, the company refused to release its clinical trial data for testing Paxil in children and adolescents, but as documented earlier in this chapter, it nonetheless used its influence with the journals and its sales force to spread the lie that the drug was safe and effective for children.

In withholding its data, the company hid behind the fact that the drug was not approved by the FDA for use in anyone under age 18 and therefore the data on testing children remained private property and could be kept secret. In taking this position, the company ignored the fact that it was surreptitiously promoting the drug, which was being widely prescribed to youth - a reality that meant doctors and
we have seen throughout this book, America’s psychiatric and medical community have consistently fought against the FDA’s label changes for antidepressants, even though they are weaker and do not call for a ban. As documented in chapter 32, organizations like the American Psychiatric Association, the Journal of the American Psychiatric Association, and the American College of Neuropsychopharmacology (e.g., Mann et al., 2006) rose up in outrage about the FDA doing anything to discourage the use of these drugs in children and adolescents.

Similarly, the press in Great Britain led the way in disclosing GSK’s corrupt practices and in calling for a ban on the prescription of antidepressants to children, while the U.S. media did little or nothing. The BBC’s Panorama helped push Britain’s regulatory agency to take action and generated enough data to warrant analysis in scientific journals (Medwar et al., 2002; Medwar et al., 2003-2004). But in the United States, the press has remained largely indifferent and at times has stood fast with organized psychiatry and medicine in its resistance to the FDA’s relatively weak measures.

What is the difference between Great Britain and the United States? Quite simply, the psychopharmaceutical complex has far greater influence in America, virtually dominating the health care industry and the media.

14.13 Britain Takes Action

The Committee on Safety of Medicines (CSM) of the British drug regulatory agency (MHRA) began a cascading assault on the SSRIs by coming down hard on the use of Paxil to treat depression in children and youth. Evidence from various clinical trials showed that episodes of suicidal behavior were between 1.5 and 3.2 times higher in children taking the drug than in those receiving placebo (Kondro, 2004).

In its September 2003 report, the CSM observed:

“An urgent meeting of the Group was convened on 4 June 2003 to consider clinical trial data which had just been received by the MHRA on the safety of paroxetine in the treatment of major depressive disorder in children and adolescents. Child and adolescent psychiatrists were invited to join the Group as visiting experts for the discussion of the data. The advice of the group informed CSM’s announcement on 10 June, that paroxetine was contraindicated in patients under the age of 18 with major depressive disorder.”

14.15 Better Than Nothing?

Goodman and Gilman’s textbook of pharmacology (Nies, 1996) warned that patients are unaware that FDA approval does not protect them from “even relatively common risks of new drugs”. Not much has changed since then, other than the criticism of the FDA has escalated. The watchdog role of the Division of Psychopharmacologic Drug Products in particular is so diluted by its friendly relationship

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As a result of these British regulatory actions, GlaxoSmithKline was forced to issue a “Dear Healthcare Professional” letter concerning the risks associated with paroxetine, trade name Seroxat in Great Britain, and confirming that the drug was contraindicated in children and youth (GlaxoSmithKline, 2003 [46]):

“A recently completed programme of clinical trials in children and adolescents under 18 years of age failed to demonstrate efficacy in Major Depressive Disorder and there was a doubling of the rate of reporting of adverse events in the paroxetine group compared with placebo, including: decreased appetite, tremor, sweating, hyperkinesia, hostility, agitation, emotional lability (including crying, mood fluctuations, self-harm, suicidal thoughts and attempted suicide).”

“Seroxat is now contraindicated in patients with major depressive disorder under 18 years of age.”

GSK would never be compelled to issue a similar warning to U.S. healthcare providers, contraindicating the drug for the treatment of depression in those under age 18.

Great Britain went on to ban all of the SSRIs for use in depression in children except for Prozac, mistakenly giving credence to two clinical trials of Prozac conducted by Graham Emsley, a close associate of Eli Lilly (chapter 7).

Canada’s regulatory agency, Health Canada (2004) [47], followed with a warning to patients of all ages taking the newer antidepressants (SSRIs, plus Wellbutrin, Zyban, and Remeron) about the risk of increased suicidality and violence (see also Kondro, 2004 [55]). The warning stated that these patients, children and adults alike, may “experience behavioural and/or emotional changes that may put them at increased risk of self-harm or harm to others”.

Notice how far the FDA has continued to lag behind Great Britain. The FDA could have declared the SSRI antidepressants to be con-

14.14 British Psychiatry Versus American Psychiatry

As already described, the British drug regulatory agency declared that Paxil was “contraindicated” for children, taking a much stronger stand than the FDA. The Royal College of Psychiatrists (2003) [73], then released a press release supporting the government’s decision:

“The Royal College of Psychiatrists welcomes the clear advice from the Medicines and Healthcare Products Regulatory Agency banning the use of Seroxat [Paxil] in children and adolescents under the age of 18 in the treatment of depressive illness.”

British medicine, including the Royal Society of Medicine, supported the ban on Paxil for treating depression in children. But as
with industry, and its total reliance on their flawed data, that it often
does more harm than good by lulling the mental health profession and
the consumer into a false sense of security in regard to the safety and
efficacy of psychiatric drugs.

The problem in regard to psychiatric drugs is compounded by the
ideology of biological psychiatry. Since its inception in state custo-
dial hospitals at the onset of the industrial revolution, psychiatry has
always promoted the medical and biological model. Claims that new
discoveries have been made that prove a biological basis for psychiatric
disorders have been going on for centuries, with little change and no
greater verification (Breggin, 1991c [19]; Moncrief, 2001 [63]).

In reality, psychiatry can claim to be like medicine, but it cannot
prove it. It can claim that depression or schizophrenia is like diabetes
or cancer, but it can offer no evidence. There are no known biological
and physical bases for the range of commonly diagnosed psychi-
tric problems, from attention-deficit/hyperactivity disorder (ADHD)
to bipolar disorder and schizophrenia.

Approving a drug for the treatment of a real physical disease, such
as pneumonia or diabetes, is very different from approving the use of
specific drugs for expressions of human suffering that are psychological,
social, and educational in origin. By giving its official imprimatur
to the use of drugs for the treatment of everything from ADHD to
schizophrenia, the FDA takes sides in the conflict between biological
and psychosocial psychiatry. It gives official government support to
biopsychiatry and to brain-disabling therapies.

What is needed? To begin with, mental health professionals, physi-
cians, and the public must become more skeptical, perhaps even cyni-
cal, and certainly more sophisticated about what psychiatric drugs
and electroshock really do to the brain, mind, and person. Awareness
of medication spellbinding and the brain-disabling principles of psy-
chiatric treatment is key to this understanding. Psychiatric drugs do
not cure mental disorders. Instead, their primary or essential effect is to cause brain dysfunction and compromise mental and emotional acuity.

Drug companies, the FDA, organized psychiatry, and other interest groups try to promote biopsychiatric interventions as grounded in good science. Instead, their widespread use defies both science and common sense and inflicts brain dysfunction and damage on millions of individuals. Unless they are responding to a placebo effect, even individuals who feel helped by the drugs are typically suffering from some degree of brain-disability and spellbinding.

14.16 A Final Word on Spellbinding

How is it that highly toxic chemicals have become so popular for the treatment of mental and behavioral problems, creating a virtual plague of brain and mind dysfunction among adults and children? One answer is contained in this chapter: drug company promotion through every conceivable avenue, including the psychopharmaceutical complex and its latest innovation, direct-to-consumer marketing. Another answer is found in human nature, the ageless search for the easy solution to the inevitable suffering and frustration of life. But none of this fully accounts for why year after year, human beings continue to imbibe substances that cause them more harm than good. That answer lies in chapter 6 in the concept of brain-disabling treatments in psychiatry, especially the newly described principle of medication spellbinding (intoxication anosognosia).

From alcohol and methamphetamine to Prozac, Valium, lithium, and Zyprexa, psychoactive substances disguise their adverse mental effects for the user. A person grossly mentally impaired by stimulants, benzodiazepine tranquilizers, mood stabilizers, or neuroleptics is likely to have little idea about how dysfunctional he or she has become.

When the individual does perceive a change in himself or herself, positive or negative, it is almost never attributed to the causative agent: the drug. If the individual feels euphoric, it is attributed to good fortune and especially to extraordinary personal attributes. If the individual feels angry or depressed, again, it is attributed to something other than the drug and usually blamed on oneself in a guilt fashion or on someone else in an angry fashion. Individuals who are given psychiatric drugs, especially stimulating ones like the newer antidepressants, often end up feeling that they are doing better than ever, when in reality their lives are falling apart. In the extreme, the drug-entranced, spellbound individuals feel compelled to act in dangerous, destructive ways that are out of character and otherwise would feel wholly alien to them.

Even sophisticated individuals, including physicians, can fall prey to medication spellbinding (Breggin, in press). While educating individual patients and the public about adverse drug effects is important, it is not a flawless defense against being driven into apathy or mania, suicide or violence, by psychiatric drugs. The answer lies in restraint - in the medical profession and the public turning away from toxic chemicals as potential solutions to the frustration and suffering that afflicts so many human beings. It also lies in looking more toward psychological, social, and educacional solutions for the wide variety of mental and emotional problems that are now so freely diagnosed and treated with drugs.
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