Report Presented at the September 14, 2004 Press Conference Sponsored by the Alliance for Human Research Protection (AHRP) at the FDA Public Hearing on Antidepressants and Suicide.

Antidepressant-Induced Suicidality and Violence: More About Deception than Science Observations Made at the FDA Hearings Press Conference, September 14, 2004

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The FDA is finally admitting that the newer antidepressants, especially the SSRIs and Effexor (venlafaxine), cause suicide in children. I first drew these conclusions about the SSRIs and began publishing them in 1994 in <u>Talking Back to Prozac</u> (Breggin and Breggin, 1994). In addition, I reviewed and analyzed the entire literature shortly before the February hearings (Breggin, 2003/2004). Ten years is a long time to wait for official recognition of such important risks. The delay in recognition has much more to do with organized deceptions than with science.

The Rate and Harmfulness of ADRS

Andrew Mosholder (2004) of the Office of Drug Safety of the FDA and others reported at these FDA hearing that 2-3 out of 100 antidepressant-treated children will develop suicidal behaviors. He also estimated that a suicidal event would occur once in every twelve patient-years. In fact, the figures are misleading and much too small. These short-term, mostly drug-company sponsored studies, were highly biased and often overlooked or ignored data concerning adverse drug effects. They were specifically aimed at proving efficacy rather than finding adverse effects and their tools for evaluating suicidal ideation and behaviors were grossly inadequate. Since some of the weaknesses in the controlled clinical trial data were described at the hearings, I will not discuss them in detail (for further discussion of clinical trial inadequacies, see Breggin 1997; Breggin and Breggin, 1994).

Furthermore, the FDA overlooked other related hazards that swell the numbers of children afflicted with serious and life-threatening adverse drug reactions. Antidepressant-induced mania is very common. The FDA-approved label for Luvox, for example, cites a rate of 4% for mania and manic-like symptoms. A controlled clinical trial by Emslie et al. (1997, p. 1003) disclosed a 6% rate of mania for children taking Prozac in a controlled clinical trial. Antidepressant-induced manic behavior can disrupt a child's life and result in injury to others. It commonly results in a false diagnosis of bipolar disorder leading to stigmatization and many years or a lifetime of unnecessary, harmful treatment with drugs.

While mentioning violence as a potential subject for investigation, the FDA did not analyze data related to antidepressant-induced violence. Experts in the field agree that suicide and violence emanate from the same basic impulses. A drug that causes suicide will also cause violence, and vice versa.

More about Deception than Science

Overall, these FDA hearings are really more about deception than about science. The FDA and the drug companies have colluded for years to hide the dangerousness of the newer antidepressants in the treatment of children and adults.

In summarizing deceptive drug company practices, I will focus on Prozac and its manufacturer, Eli Lilly. Much of the following information was developed in my role as a medical expert in product liability suits against the manufacturer, beginning in the early 1990s when I was the scientific investigator and medical expert for the hundreds of combined Prozac suits. All of the suits in which I have been involved have been settled. In addition, I have similar information in regard to other SSRI manufacturers, but much of that information has been sealed after settlements in various suits.

Here is a brief summary of some of the ways that Eli Lilly, often in collaboration with the FDA, has hidden data on the dangerousness of the SSRIs (many of these deceptions are discussed in Breggin and Breggin, 1994, and all of them are documented in Breggin, 1997):

- (1) In the last few days before the FDA approved Prozac marketing, Bob Temple of the FDA went through the Prozac label and drew lines through adverse drug reactions that he considered superfluous. He specifically expunged "depression" from the list of <u>frequently</u> reported psychiatric adverse drug reactions. Thus, "depression" as a drug-induced effect went from frequent to nonexistent in the drug label. The information that depression was a "frequent" reaction to Prozac had poured into Eli Lilly and Company from principal investigators funded by the company to do clinical trials, but recognition of its existence was eradicated.
- (2) Psychiatrist Richard Kapit, the FDA's chief medical officer for safety in the evaluation of Prozac, concluded that the drug had a "stimulant profile"—including insomnia, agitation, over-stimulation, and weight loss—that could worsen depression. He warned about this risk in his safety summaries and at the PDAC meeting. He called for the label to be modified to include a warning that the drug acts like a stimulant and can worsen depression. He also mentioned reports of suicide and murder in patients taking Prozac. Both the FDA and Eli Lilly and Company rejected Kapit's repeated warnings.
- (3) In response to German concerns about increasing suicide rates among Prozac patients, the drug company tallied all the reports of suicide attempts. It found a statistically significant increased rate of suicide attempts among Prozactreated patients compared to patients treated with placebo or older antidepressants in all of the company's controlled clinical trials. Prozac patients were six times more likely to have suicidal behavior. After generating this data and having it evaluated by an outside consultant, Eli Lilly hid the data from the German agency and from the FDA. I found the memorandum and the data while doing discovery as the scientific investigator for the combined Prozac suits. I testified about the data in the Wesbecker case (Fentress et al., 1994) and published it in my books (Breggin, 1997).

The FDA and the drug company have never responded to these disclosures. In fact, Tom Laughren of the FDA stated at the public hearing yesterday that there were no data demonstrating an increased suicidality risk for adults taking SSRIs and I reminded him about this data in my testimony at the hearing.

- (4) In response to German concerns about the stimulating effects of Prozac, Eli Lilly and Company reanalyzed their data from the clinical trials and found that 38% of Prozac-treated patients displayed some symptoms of "activation." In fact, the figures would have been higher if the company definition of activation had not been narrow (excluding even manic-like symptoms) and if many of the patients hadn't been tranquilized with benzodiazepines.
- (5) Eli Lilly and Company hid Prozac-induced suicidal behavior by coding suicide attempts under misleading terms such as "no drug effect." As a result, when researchers or investigators searched the company's records or the FDA's records, these suicide attempts were not discoverable. I testified about this deception in 1994 and wrote about it in my books (Breggin, 1997); but the FDA and the drug company have never responded to these disclosures.
- (6) Eli Lilly eliminated akathisia from the codes that could be used by its principal investigators to identify and categorize Prozac-induced adverse drug effects in the clinical trials. This deception is very important because even the DSM-IV and DSM-IVTR now recognize that SSRIs cause akathisia, and that akathisia can result in suicidal and violent behavior. Instead of being coded as akathisia, these events were put in misleading categories such as agitation and hyperactivity. I testified about this in 1994 and described this deception in my books, but again the FDA and the drug company have not responded.
- (7) The FDA conducted an epidemiological study comparing rates of violent behavior for Prozac and another antidepressant, trazodone. The reports were drawn from the FDA's spontaneous reporting system that includes all events reported to the drug company and the FDA. The FDA found greatly increased reporting rates for violence on Prozac even when taking into account the higher number of prescriptions for Prozac. Also, the increased rate of violence reports began even before there was publicity and controversy surrounding the problem. When I attempted to obtain this data from the FDA, the agency told me it had been lost. However, I was able to obtain the data in the form of charts from the drug company through discovery. I testified about this in 1994 and published it in my books, but again the FDA and the drug company have not responded.
- (8) Prozac failed to demonstrate efficacy in its clinical trials. When this potential economic disaster for Eli Lilly and Company was discovered, the FDA offered a way out to the drug company. The FDA allowed the drug company

to include in its efficacy data those patients who had been illegally treated with concomitant benzodiazepine tranquilizers in order to calm their overstimulation. With these patients included, statistical manipulations enabled the FDA to find the drug marginally approvable. Basically, Prozac was approved in combination with addictive benzodiazepines such as Ativan, Xanax, and Valium; but neither the FDA nor the drug company revealed this information.

To repeat, much of the documentation for these observations has been presented in my testimony in the Wesbecker case (Fentress, 1994) and in <u>Talking Back to Prozac</u>, and all of it is documented in <u>Brain-Disabling Treatments in Psychiatry</u> (Breggin, 1997). More general discussions can also be found in <u>The Antidepressant Fact Book</u> (Breggin, 1992). I have additional data and deceptions concerning other SSRI-manufacturers but much of it is sealed by court order, and the FDA has shown no interest in learning about it.

Over the past two days, the FDA has repeatedly said that it didn't have specific answers to questions that I have already researched as a medical expert in product liability suits. For example, it was asked whether or not suicidal behavior was correlated with stimulant adverse effects such as agitation and akathisia. The FDA responded that this tedious, time-consuming analysis had never been done. However, I have done it in product liability suits where I have documented a clear relationship between suicidal behavior and stimulant side effects. The FDA has shown no interest in obtaining this data from me. The drug companies involved have kept the information hidden or under seal.

I have also found data confirming that the worst stimulant adverse effects often occur in the first few days or weeks of treatment, explaining the increased rate of suicidal behavior during this period of time. Again, the FDA has shown no interest in this data and some of it remains sealed.

Finally, the FDA has insisted on requiring confirmation from controlled clinical trials before admitting that antidepressants can cause suicide. This has been a massive subterfuge. In the past, when the FDA has increased the severity of warnings for psychiatric drugs or withdrawn them from the market, the agency has almost always relied upon increased numbers of clinical reports in combination with a general medical analysis of the potential problem. On this basis, the capacity of Prozac to cause violence and suicide has been known since the 1980s, and was clearly documented in my books as early as 1994.

The FDA has colluded with the drug companies in hiding the dangers of the antidepressant medication. The risk of suicide in children is but the tip of the iceberg that includes high rates of antidepressant-induced suicide, violence, overstimulation, and mania.

Addendum

Following the press conference, two major events occurred:

First, Robert Temple of the FDA acknowledged at the public hearing that "causality" has now been established concerning the link between antidepressants and

suicidality in children. This should end any challenges to the "science" in criminal, malpractice, and product liability suits.

Second, the FDA committee recommended a black box warning concerning suicidality in antidepressant labels. However, the FDA has stated its intention to place the label on all antidepressants, thus watering down the impact on the sales of SSRIs and Effexor, the worst offenders. In addition, the label will be placed on antidepressants that have not been FDA-approved for any use in children, indirectly suggesting the possibility of their prescription to children. Short of banning these offending medications, the FDA should make these drugs contraindicated in children. A contraindication would make clear that these drugs should not be prescribed to children, but the FDA is unlikely to take such a strong stand against its allies in the drug industry.

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