



Statement of Diana Zuckerman, Ph.D.
President, National Research Center for Women & Families
Before the FDA Psychopharmacologic Drugs Advisory Committee

June 9, 2009

I am pleased to have the opportunity to testify as president of the National Research Center for Women & Families. Our nonprofit research and education center does not accept contributions from companies that make medical products that we evaluate, or competing companies, and so I have no conflicts of interest.

My doctorate is in clinical psychology and my post-doctoral training at Yale was in psychiatric epidemiology and public health, and I have clinical and research experience with patients with depression, bipolar disorder, and schizophrenia. Prior to my current position, I was on the faculty at Yale and Vassar, a study director at Harvard, and worked in the U.S. Congress and the Public Health Service. I have worked on FDA issues for 19 years.

Our Center is dedicated to improving the health and safety of adults and children, and we do that by scrutinizing medical and scientific research to determine what is known and not known about specific treatments, and to compare their safety and effectiveness.

In addition, I am a fellow at the University of Pennsylvania Center for Bioethics.

I was very glad to hear the newly confirmed FDA Commissioner talk about the need to refocus the FDA on its public health mission. This meeting is a great place to start. That's your task today.

I was therefore very disappointed by the quality of the research presented for these three drugs, and the FDA's failure to clearly present those shortcomings in today's meeting.

The key question is: Do the benefits outweigh the risks for the 3 drugs under consideration today for children with either schizophrenia or bipolar disorder?

That question must be considered in the context of the risks and benefits of other drugs that are available. And since all 3 drugs are already on the market and widely used off label for children, the other question is: Would FDA approval send an inappropriate message of safety that is not supported by the research?

Based on the documents provided to all of us, some FDA officials seem ready to approve these drugs for children. **That should not influence your task today.** Your task is to carefully and independently scrutinize the scientific data, to consider the impact of approval, and to decide **whether any or all of these 3 drugs are proven safe and proven effective for adolescents, compared to other available products.**

Remember that the FDA asked the companies to do these studies on children, and in exchange for these studies, each of the companies received a patent extension on these drugs worth many millions of dollars – much more than the cost of these studies. The companies have already benefited greatly from these studies, whether these drugs are approved for children or not. You don't need to worry about hurting their feelings. You need to determine if they have done right by America's children – and our nation's psychiatrists – by proving long-term safety and effectiveness. Unfortunately, they haven't.

The studies are inadequate. The study samples are too small. The double blind studies are too short—3-6 weeks long, and even the open label studies are less than one year. In contrast, schizophrenia and bipolar disorder last for decades, often for life, and treatment is needed during all those years.

These studies provide almost no useful information about long-term adverse reactions such as tardive dyskinesia, sudden death, or diabetes. However, there is a growing research literature, including numerous studies published in the past year, which show how high those risks are likely to be. And, even the short-term studies prove the very substantial risk of weight gain, sedation, and several other potentially debilitating side effects.

The known risks are much too high to justify approval for bipolar disorder. Lithium is a safer alternative, as well as less expensive and more effective. Two other atypical antipsychotics are also FDA approved for children, and although they have many similar risks, that is NOT a reason to approve these 3 drugs. Remember, these 3 drugs would still be available, for use off label, if other treatments don't work. There is no reason to approve them at all, not even as second line drugs, because advertising would inevitably and inappropriately turn them into first line choices.

What about children with schizophrenia? Do the benefits outweigh the risks? It's impossible to answer that question because these studies are too small and too short-term to provide useful information about either the risks or the benefits. The FDA should have demanded more, but they didn't. So, the FDA needs to demand more now. And, you need to make sure that they do.

Here's just one example: Isn't it obvious that kids in the Russian Zyprexa placebo group knew that they were receiving placebo? That's the logical explanation for why the Russian kids showed no placebo effect and almost two-thirds of the kids dropped out of the placebo group in that study. Compare those results to *any other study* of atypical antipsychotics and you'll see that the results are much different. The FDA reviewer was absolutely right to reject those data as suspicious, and FDA should have respected those concerns. This committee should too.