Scientific Panel
MindFreedom Support Coalition International
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20 September 2004

Cathryn M. Clary, MD, MBA, Vice President
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Dear Dr. Clary:

David Oaks, Executive Director of MindFreedom Support Coalition International has asked us to review your letter of response to our letter of April 16, 2004 and to reply to it.

In your response you have again failed to answer our questions. You cite two articles from peer-reviewed scientific journals. One is an article entitled "Neurobiology of Serotonin in Depression and Suicide" by Stockmeier in Volume 836 of the Annals of the New York Academy of Science.

Stockmeier discusses several different avenues of research suggesting that serotonin alterations are implicated in clinical depression. For instance, he notes there have been 12 studies that examined the postmortem brains of suicide victims, but he also points out that some studies found an increased number of serotonin receptors while some studies found no changes. Stockmeier's conclusion: "The current results suggest that the number of serotonin–1A and serotonin–2A receptors in the right prefrontal cortex or hippocampus are not altered in suicide victims with major depression." (p. 223). In short, at best, Stockmeier talks about some interesting possibilities but offers little in the way of specifics to back up your claims.

You include the following quote from Stockmeier's article:

> "Powerful evidence of an imbalance in serotonin neurotransmission in major depression comes from the observation that the symptoms of this disorder are relieved by repeated treatment with drugs that block the reuptake or metabolism of serotonin."

The use of the word “imbalance” in that quote is a breach of scientific protocol in that it exaggerates and misrepresents what was actually demonstrated by the research reported in the article. The research merely demonstrated that a psychotropic drug had an effect on the reuptake and metabolism of serotonin. To say that is evidence of “an imbalance in serotonin neurotransmission” is erroneous because nobody has demonstrated what the balance of serotonin transmission is in the healthy human brain. This is not quibbling or nitpicking. Determining the balance of serotonin in the healthy brain would be a great scientific breakthrough. Unfortunately, we haven’t succeeded in achieving that breakthrough yet. In the absence of that knowledge, to claim as you do in your advertising that Zoloft “helps correct the chemical imbalance of serotonin in the brain” is a misrepresentation of the truth.

The quote bases the evidence of imbalance on the “observation that the symptoms of this disorder are relieved by repeated treatment with drugs that block the reuptake or metabolism of serotonin.” We would point out that the symptoms of depression are also relieved by cocaine, heroin, methamphetamines and marijuana. As you know, all of those drugs also inhibit the reuptake of neurotransmitters, including serotonin. And they all have very damaging side effects on human beings. Using the scientific principle of parsimony, we would infer that the psychotropic drugs your firm manufactures and sells have similarly damaging side effects. And, as you also know, there is evidence that your drugs do increase the risk of violence and suicide in people who use them, do inhibit sexual functioning and do create problematic tolerance and withdrawal effects in users. In fact, after its February, 2004 hearing on the impact of SSRI use on suicidal ideation and behavior in children and adolescents, the United States Food and Drug Administration ordered drug companies to add warnings of these dangerous side effects to their drug labels.

In your letter you cite a textbook by Stephen A. Stahl entitled *Essential Psychopharmacology: Neuroscientific Basis and Practical Applications*. This is a textbook that discusses the mechanism of action of many psychotropic drugs. It is an interesting book but it hardly serves as documentation of a biological basis of mental illness. Here are two quotes taken directly from the book:

> “No single reproducible abnormality in any neurotransmitter or in any of its enzymes or receptors has been shown to cause any common psychiatric disorder. Indeed it is not longer considered likely that one will be found, given the complexity of psychiatric diagnosis and the profound interaction of environmental factors with genetics in psychiatric disorders.” (p. 103).
>
> “Since it was recognized by the 1960’s that all the classical neurotransmitters boost NE, DA and SHT in

> one manner or another, the original idea was that one or another of these neurotransmitters, also chemically known as monoamines, might be deficient in the first place in depression. Thus, the 'monoamine hypothesis' was born. A good deal of effort was expended, especially in the 1960's and 1970's, to identify the theoretically predicted deficiencies of the monoamine neurotransmitters. This effort to date has unfortunately yielded mixed and sometimes confusing results." (p. 45)

Stahl's conclusions seem very different from the standard advertising slogans that are used to sell SSRI's.

In your letter you also cite an article entitled "The Serotonin Transporter: A Primary Target for Antidepressant Drugs" by Schloss and Williams in Volume 12 of the Journal of Psychopharmacology and include the following quote:

> "Decreased serotonergic neurotransmission has been proposed to play a key role in the aetiology of depression. The concentration of synaptic serotonin is controlled directly by its reuptake into the pre-synaptic terminal and, thus, drugs blocking serotonin transport have been successfully used in the treatment of depression….The therapeutic effect of SSRI antidepressants is thought to result from an enhancement of 5-HT neurotransmission due to long-lasting adaptive changes in serotoninergic neurons."

In this quote, the use of the phrase "key role in the aetiology of depression" is another breach of scientific protocol, another case of exaggeration and misrepresentation. In fact, there is no evidence that decreased serotonergic neurotransmission has any role at all in the aetiology of depression. There is only evidence that when some human beings ingest a drug that has an effect on the reuptake of serotonin, they experience relief from the symptoms of depression. That is only evidence of a correlation between ingesting a substance and relief of symptoms. It says nothing about the aetiology of the symptoms. Correlation does not constitute causality. A causal relationship must be proven by other than statistical correlation, a standard which biopsychiatry has yet to meet.

As we pointed out in our last letter, we agree that Zoloft and the other SSRI's act on the serotonin receptors. Although you continue to state that this is the heart of the disagreement, it is not. What we disagree about is your continued reference to evidence proving that psychological distress **results** from altered neurotransmitter levels. You continue to talk about these two ideas in the

same sentence implying that, if evidence documents that Zoloft acts on the serotonin receptor, then that same evidence somehow proves that depression must be **due** to a shortage of serotonin. We have received four letters responding to our request for scientific evidence that mental disorders are "biologically-**based** brain diseases" and not a single letter has provided any specific citations to support that claim.

We believe the aetiology of depression resides in the cognitive, emotional and somatic experience of individuals as they struggle to create meaningful and satisfying lives and that the biochemical dynamics on which your drugs work are mediating rather than causative variables.

In fact, the Schloss and Williams article is a somewhat speculative review of research on the molecular structure of the serotonin transporter and the chemical and electrical characteristics of the serotoninergic system. It contains frequent use of words such as "putative" (assumed to exist or have existed), "possible" and "proposed." On page 115 of the article, the authors write:

> "The direct mechanisms underlying inhibition of (serotonin) transport as well as the long-term, mood-modulating effects of these drugs are, however, not yet understood."

Reading the article leads one to question the wisdom of ingesting a drug which affects a complex, intricate and critically important organic system about which so little is known.

In your letter you say it is disingenuous of us to not have disclosed our conflicts of interest. Apparently you consider clinical trial researchers' undisclosed receipt of millions of dollars from pharmaceutical companies, on the one hand, and efforts to advocate for victims of harmful drugs and to study human health independently, on the other, as equivalent conflicts of interest. Now that is truly disingenuous. Given the vast influence of drug companies over academic medicine and clinical biopsychiatry, our questioning of the science behind biopsychiatry actually limits our career opportunities.

The misrepresentation exhibited in the quotes and article you have offered is precisely what we object to. Through such statements, you create the impression that biopsychiatry and the widespread prescription of psychotropic drugs rest on a solid scientific foundation. Unfortunately, the media and much of the public have been fooled by you. We haven't been and we think it is important that we share our skepticism and concern as widely as possible.

We don't impugn the fundamental motivation of Pfizer, Inc and other pharmaceutical companies. However, we believe that, by continuing to misrepresent current scientific knowledge you are doing a disservice to human

beings and harming rather than helping their efforts to achieve better levels of health and well-being.

Specifically, your web site contains the following statement:

> "Although the way Zoloft works for depression, panic disorder, OCD and PTSD is not completely understood, what is understood is that Zoloft is a medicine that helps correct the chemical imbalance of serotonin in the brain."

We have asked you repeatedly for scientific evidence to support that statement. You have sent us citations of textbooks and articles which fail to meet the test of any established scientific standards to demonstrate the truth of that statement. We, therefore, conclude that your statement is not a true statement and wonder why you justify continuing to state it.
Sincerely,

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David Cohen, PhD
Ty Colbert, PhD
Pat Deegan, PhD
Al Galves, PhD
Tom Greening, PhD
Keith Hoeller, PhD
David Jacobs, PhD
Jay Joseph, PhD
Jonathan Leo, PhD
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