Concerning CDC's Analysis
Increase in child/adolescent suicides from 2003 to 2004

According to an analysis conducted by the Centers for Disease Control (CDC), titled "Annual Summary of Vital Statistics: 2005" and published in the journal PEDIATRICS on February 2, 2007, there was an 18% increase in suicides from 2003 to 2004 (31,484 or 1.3% in 2003 and 32,439 or 1.4% in 2004).

While the CDC authors draw no conclusions as to the meaning or possible cause of the increase, the pharmaceutical industry and its apologists have seized upon the data as an opportunity to blame the FDA's black box warnings concerning the increased risk of suicidality in children and adolescents taking antidepressants. Long-time champions of the use of antidepressants and other drugs to treat children and adolescents have come out of the woodwork to blame the black box. In evaluating these claims, the following should be kept in mind:

What CDC Scientists say about their own study:

According to fdanews.com: "[W]hile the suicide increase coincides with the FDA's decision to require black box warnings on SSRIs, **this does not necessarily mean that the warnings led to more suicides** Arialdi Minino, a NCHS statistician said." In fact, according to the CDC scientist: **"The fact that the rates were even higher between 1999 and 2001 lends doubt to the theory that black box warnings are the cause."**

"The data would be more significant if the rates were flat before the black boxes," he added.

"**The CDC** will be issuing a more detailed report later in the year, and in the meantime **are urging people not to jump to conclusions about the cause of this sudden 'spike' in the data.** Nobody knows yet whether this sudden rise is concentrated in certain parts of the population, for instance ethnically or geographically that might lead to other explanations."

Also, keep in mind:

1) The bias and vested interest of those proclaiming that the black box is the cause of the increase in suicide rates between 2003 and 2004. Almost all of the "scientists" speaking out about the black box and its relationship to rising suicide rates have a vested interest (including an interest in defending their own actions of promoting the use of the drugs for children and adolescents despite an absence of efficacy data) and most have pharmaceutical industry ties.

2) The FDA's analysis, which found that antidepressants cause an risk of suicidality in children and adolescents **was not announced until a September 2004** Psychopharmacologic Drugs Advisory Committee (PDAC) meeting. The FDA did not

ask the manufacturers of antidepressants to place black box warnings in their labels until **October 2004.**

3) The black box warnings did not go into effect until **January/February 2005**, well beyond the CDC analysis time period.

4) Conflicting and inconsistent data.

According to a February 2005 report in the Washington Post:

> Various studies have shown a three- to tenfold rise in the use of antidepressants among children between 1987 and 1996, and an additional spike of 50 percent between 1998 and 2002. There was a further increase of about 9 percent between 2002 and 2003, but the new data revealed a 10 percent decline last year [2004], said Robert Epstein, chief medical officer at Medco.

However, according to Psychiatric Services, News & Notes, Oct. 2004 Vol. 55, No. 10:

> In 2003, U.S. physicians wrote 15 million antidepressant prescriptions for patients under age 18, according to FDA data. **In the first six months of 2004, antidepressant prescriptions for children increased by almost 8 percent, despite the new drug labeling.**

The first FDA advisory committee meeting concerning a possible increased risk of suicidality with children and adolescents taking antidepressants took place on **February 2, 2004.** The FDA issued a Public Health Advisory concerning the risk of antidepressant-induced suicidality on **March 22, 2004.**

When considering all of these figures and suicide trends in the time frames noted above, the theory that black box warnings are the cause of the "spike" in suicide rates, as the CDC itself has pointed out, simply does not hold up.

5) Similar arguments have been made, but to no avail.

When Milane and Lucinio et al. made a similar argument – that the temporal patterns of Prozac prescriptions and suicide rates suggested that Prozac had saved "thousands of lives," Stanford University epidemiologist Carlos A. Camargo and colleague Daniel A. Bloch were less than impressed, calling the suggestion "an elaborate edifice."

They correctly pointed out that "Suicide is the final outcome of many conditions, and there have been, for many decades, scholarly articles indicating the many risk factors which increase the likelihood of suicide: poverty, loss of employment, and several other economic indicators have been shown to have a strong effect upon suicide rates ... In the 1990s there was a very substantial and prolonged improvement of the US economy [], which could partially explain a lowering of the suicide rate" during the 1990s.

The authors concluded:

> [W]e believe that there is little likelihood that the increasing sales of [Prozac] from 1988 to 2002 were the cause of the modest decrease in the suicide rate during those years. It appears more likely that factors such as those connected with the sustained economic recovery of the 1990s were responsible.

In an illustrative corollary, the authors noted: "We doubt that many will advance the thesis that the increasing sales of [Prozac] were, somehow, one of the causes of the rise of the Dow Jones index."

6) Failure to consider lack of efficacy. The drugs have not been shown to be an effective treatment for childhood/adolescent depression, so why would rising suicide rates be related to their declining use? Quite frankly, it's surprising the rate of antidepressant prescriptions for children hasn't declined even more dramatically given the drugs have repeatedly failed to demonstrate efficacy in this population.

As one of the FDA advisory committee members who voted for black box warnings (Dr. Thomas Newman, an epidemiologist and pediatrician from the University of San Francisco) stated:

> We have I think very strong evidence of harm and really not very good evidence of efficacy ... You bring people in, you start a medication, and you see an improvement, you are very, very likely to believe that the drug is effective, and the reason why we do randomized, double-blind trials is because personal experience, however compelling, is not a reliable way to tell whether drugs work.

Dr. Newman later articulated his point when he wrote:

> It is easy to see why the personal experience of clinicians and patients would lead them to believe the drug to be effective, since they would have no way of knowing that more than 85 percent of the benefit they observed would also have occurred with placebo.

In fact, the lack of proof of effectiveness was a consistent theme throughout both FDA advisory panel meetings, in February and September 2004, as well as at the Congressional hearings that took place in September 2004 concerning the FDA's handling of the antidepressant suicide issue.

There was even considerable discussion during the 2004 PDACs that language concerning the failure of the drugs to demonstrate efficacy should be included in the black box. For whatever reason, the issue later disappeared from the radar screen.

Medications have levels of efficacy. In the risk benefit analysis, physicians and their patients have the right to know how effective the treatment is for their particular

condition and compare that with the risks so they can decide whether it's worth it or not. Otherwise, how is a proper risk benefit analysis to be done?

A case in point is Prozac, the one antidepressant in the group subject to the black box warnings that has been approved by the FDA for depression in pediatric patients. As Dr. Thomas Newman explained, "if you look very closely at the [Prozac] trial, just as an example, at the Childhood Depression Rating Scale, the improvement with placebo was 19 points, and the improvement with the drug was 23.4 points ... the improvement over placebo was really very, very small, and I would say not detectable by a clinician treating individual patients. ..."

The FDA itself is aware of this. Dr. Paul Leber, formerly of the FDA, expressed some trepidation over approving Zoloft as an effective treatment for depression when he stated in a 1991 FDA internal memorandum: "Approval [of Zoloft] may ... come under attack by constituencies that do not believe the agency is as demanding as it ought to be in regard to its standards for establishing the efficacy of antidepressant drug products."

7) There is no scientific evidence that shows antidepressants prevent suicide. Companies generally argue that only controlled clinical trials can answer questions concerning what is causing a particular outcome.

In fact, the double blind placebo controlled clinical trials show that antidepressants do not prevent suicide. According to a study by Gunnel et al.: "Surprisingly, direct evidence that antidepressants prevent suicide is hard to find. ... In the most comprehensive synthesis of data from randomised trials, Khan and colleagues found no evidence of a beneficial effect of antidepressants on suicide." Gunnell, citing Khan A, Khan S, Kolts R, Brown WA. "Suicide rates in clinical trials of SSRIs, other antidepressants, and placebo: analysis of FDA reports," Am J Psychiatry 2003;160: 790-2. Gunnel et al., "Antidepressants and suicide: what is the balance of benefit and harm," British Medical Journal (BMJ), 2004; 329:34-38 (3 July)

According to another study, by Herman Van Praag, published recently in World Journal of Biological Psychiatry titled "A Stubborn Behaviour: the Failure of Antidepressants to Reduce Suicide Rates," despite the increased use of antidepressants "completed suicide has remained quite stable" and "suicide attempts even seem[] to have increased."

8) The current trend in suicides for children and adolescents could be the result of the meteoric rise in pediatric prescriptions of atypical antipsychotics, such as Zyprexa and Risperdal.

According to research conducted by Medco Health Solutions, Inc., in which the company reviewed prescription drug claims of some 370,000 youngsters ages 10 to 19, the prevalence of adolescent girls taking antipsychotics has grown 117 percent in the past five years while it has increased 71 percent for boys. The suicide rates are even higher in patients taking antipsychotics than those on antidepressants.

Dr. Arif Khan of the Northwest Clinical Research Center in Bellevue Washington, in August 2002, reported "an analysis of clinical trial data for drugs approved by the Food and Drug Administration between 1985 and 2000. This included suicide and attempted suicide rates for more than 71,604 patients treated with the atypical antipsychotics ...and ... all the selective serotonin reuptake inhibitors ... and [an] anticonvulsant."

"One striking finding was the elevated rate of completed suicides for patients during these trials. Compared with the rate of 11/100,000 persons per year for the population at large, the rates of completed suicide were 752/100,000 persons per year for those in antipsychotic trials for such drugs as risperidone (Risperdal), olanzapine (Zyprexa); 718 in antidepressant trials; 425 in trials of medication for social anxiety disorder; 136 for panic disorder; and 105 for obsessive-compulsive disorder."

According to Khan, "[t]his was particularly surprising in light of the attempt, in most clinical trials, to exclude patients who are actively suicidal." Dr. Khan concluded, "We have to ask if medication is the only way to approach the prevention of suicide." http://www2.eclinicalpsychiatrynews.com/scripts/om.dll/serve

9) Effective treatment does not necessarily mean medication.

As Dr. David Healy, a Professor of Psychiatry at the University of Wales stated recently, **"Physicians have lost confidence in their own ability to help patients without drugs."** Perhaps that is why some doctors are frantically fighting to turn back the clocks of time on the black box warnings and seem to be against informed choice. They've become so dependent on having an arsenal of "quick-fix" pills, they can't imagine not using them. And, perhaps they can't stand the idea that they might have been wrong all these years. Who could blame them? Think of the implications.

They've convinced themselves that these kids need their medications – medication is the only answer -- and that, without them, they will suffer, perhaps even die. **But the scientific evidence simply does not support this conclusion.** While they insist there must be an abundance of "scientific evidence" to prove the drugs are unsafe and lament that anecdotes hold no weight, **they reject scientific evidence that shows the drugs are ineffective.**

Something Carl Sagan said 20 years ago seems to apply here:

> One of the saddest lessons of history is this: If we've been bamboozled long enough, we tend to reject any evidence of the bamboozle. We're no longer interested in finding out the truth. The bamboozle has captured us. It is simply too painful to acknowledge -- even to ourselves -- that we've been so credulous.

Carl Sagan, "The Fine Art of Baloney Detection," Parade, February 1, 1987.

10) There are alternatives.

Medication is not the only means of "treatment." All medications have risks and in the case of antidepressants, the risks are not just limited to suicidal thoughts and behavior. There are alternatives that should be considered, particularly with children whose bodies and minds are still developing.

According to recent studies from the UK, exercise in a green environment is one effective means of combating depression. In response to the high cost of drugs, the rise in prescriptions and the fact that 93 percent of GPs reported that "they have prescribed antidepressants against their better judgment owing to the lack of alternatives," two new studies conducted in the UK found that "participating in green exercise activities provides substantial benefits for health and wellbeing." The "green activities" included gardening, walking, running and bicycling, particularly in a "green" environment.

Patients have the right to make informed choices about the risks and benefits of the medications they take. In today's managed care environment, more and more, patients are taking charge of their own health. They need information in order to make the right choices for themselves.